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**In the Claims**

Please cancel claim 31 and add new claims 89 and 90 as indicated in the listing of claims below pursuant to 37 C.F.R. §1.121.

1. (Original) Isolated nuclear protein which binds, in a sequence specific manner, to a transcriptional regulatory DNA element of an immunoglobulin light chain genes, a transcriptional regulatory DNA element of an immunoglobulin heavy chain genes or both.
2. (Original) Isolated nuclear protein, which binds, in a sequence specific manner, to enhancer DNA sequences of the kappa light chain gene.
3. (Original) A nuclear protein of claim 2, wherein the sequences are TGGGGATTCCCA.
4. (Original) Isolated NF- $\kappa$ B.
5. (Original) Isolated nuclear protein, which:
  - a) binds to DNA sequences in the upstream region of both mouse heavy and Kappa light chain gene promoters; and
  - b) binds to DNA sequences of mouse heavy chain gene enhancer.
6. (Original) A nuclear protein of Claim 5, wherein the sequences are ATTTGCAT.
7. (Original) Isolated nucleic acid encoding a nuclear protein of Claim 1.
8. (Original) Isolated nucleic acid encoding a nuclear protein which binds, in a sequence specific manner, to enhancer DNA

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sequences of the Kappa light chain gene.

9. (Original) Isolated nucleic acid of Claim 8 wherein the nuclear protein binds, in a sequence specific manner, to enhancer DNA sequences of the Kappa light chain gene.
10. (Original) Isolated DNA encoding a structural gene for a nuclear protein, which protein binds in a sequence specific manner to the kappa enhancer.
11. (Original) Isolated DNA which encodes a nuclear protein which:
  - a) binds to DNA sequences in the upstream region of both mouse heavy and Kappa light chain gene promoters; and
  - b) binds to DNA sequences of mouse heavy chain gene enhancer.
12. (Original) DNA encoding the transcriptional regulatory factor IgNF-B (NF-A2).
13. (Original) A cloned DNA sequence which encodes a protein which binds to the  $\kappa$ -element TGGGGATTCCCCA and which hybridizes to a single, approximate 10kb RNA transcript from both B and non-B human cells.
14. (Original) An assay for detection of binding of cellular nuclear protein to DNA, comprising the steps of:
  - a) providing an extract of cellular nuclear protein;
  - b) preparing an incubation mixture consisting of:
    - i) the extract of nuclear protein;
    - ii) a radiolabeled DNA fragment to be tested for binding with the nuclear protein; and
    - iii) an alternating copolymer duplex poly(dI-dC)-

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poly(dI-dC);

- c) incubating the mixture under conditions which allow the formation of protein-DNA complexes; and
- d) resolving complexed DNA from free DNA by electrophoresis through a low ionic strength, nondenaturing polyacrylamide gel.

15. (Original) An assay of Claim 14, wherein the radiolabeled DNA fragment to be tested is less than about 100 base pairs.

16. (Original) A method of Claim 14, wherein the DNA fragment is end-labeled with  $^{32}\text{P}$ .

17. (Original) A method of enhancing the transcription of a gene of interest whose transcription is regulated by a regulatory factor which binds DNA in the vicinity of the gene, comprising the steps of:

- a) preparing an expressible gene construct comprising a strong promoter linked to a gene encoding the regulatory factor; and
- b) incorporating into a cell containing the gene of interest, single or multiple copies of the gene construct sufficient to enhance transcription of the gene of interest.

18. (Original) A method of Claim 17, wherein the cell is a lymphoid cell and the gene of interest is a gene encoding an Ig chain.

19. (Original) A method of Claim 17, wherein the regulatory factor is selected from the group consisting of the following factors: IgNF-A, E, IgNFB and NF- $\kappa$ B.

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20. (Original) A method of Claim 17, wherein the regulatory factor is IgNF-B.
21. (Original) A method of Claim 17, wherein the lymphoid cell is a hybridoma cell.
22. (Original) A method of enhancing transcription of a gene encoding an Ig chain, comprising:
  - a) preparing an expressible gene construct comprising a strong promoter linked to DNA encoding a structural gene for B-cell nuclear protein, which protein binds in a sequence specific manner to a transcriptional regulatory DNA element of an immunoglobulin light chain genes, a transcriptional regulatory DNA element of an immunoglobulin heavy chain gene or both; and
  - b) transferring an Ig chain-producing lymphoid cell with the construct in multiple copies to enhance the transcription of the Ig chain-encoding gene.
23. (Original) A method of claim 22, wherein the DNA encoding the structural gene for a B-cell nuclear protein encodes IgNFB.
24. (Original) A lymphoid cell transformed with an expressible nucleic acid construct comprising nucleic acid encoding a transcriptional regulatory factor which regulates Ig gene transcription.
25. (Original) A lymphoid cell of claim 24, which is a hybridoma.
26. (Original) A lymphoid cell of claim 24, wherein the regulatory factor is B-cell nuclear protein, which protein

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binds in a sequence specific manner to a transcriptional regulatory DNA element of an immunoglobulin light chain gene, a transcriptional regulatory element of an immunoglobulin heavy chain gene, or both.

27. (Original) A lymphoid cell of claim 26, wherein the regulatory factor is IgNF-B or NF- $\kappa$ B.
28. (Original) A method of screening for the expression of a sequence-specific binding protein by a recombinant expression vector, comprising contacting protein produced by a host cell transformed by the recombinant vector with a nucleic acid recognition site probe, under conditions which permit the specific formation of a complex of the sequence-specific binding protein and the recognition site probe and determining whether such formation of a complex occurs, wherein formation of a complex is an indication of the expression of the sequence-specific binding protein by the recombinant vector.
29. (Original) A method of identifying recombinant expression vectors which express a sequence-specific DNA binding protein, comprising the steps of:
  - a) cloning the vector in host cells to form clonal colonies;
  - b) generating a replica plate of the cellular protein of the clonal colonies;
  - c) contacting the cellular protein with a DNA probe comprising a DNA sequence embodying the binding site of the sequence-specific binding protein under conditions which permit the sequence specific binding protein to bind the probe to form a complex; and
  - d) washing the cellular protein to remove unbound probe.

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30. (Original) A method of claim 29, wherein the sequence-specific binding protein is a transcriptional regulatory factor.
31. (Canceled)
32. (Original) A method of claim 29, wherein a nonspecific competitor DNA is contacted with cellular protein along with the DNA probe.
33. (Original) A method of claim 32, wherein the nonspecific competitor DNA is poly(dI-dC)-poly(dI-dC) or denatured calf thymus DNA.
34. (Original) A method of claim 29, wherein the probe is up to 150 bp in length.
35. (Original) A method of claim 29, wherein the probe comprises a oligomer of binding sites for the sequence-specific binding protein.
36. (Original) A labeled DNA probe complementary to at least a portion the sequence of nucleic acid encoding a transcriptional regulatory factor.
37. (Original) A DNA probe of claim 36, wherein the factor is lymphoid-specific.
38. (Original) A DNA probe of claim 37, selected from the group consisting of NF- $\kappa$ B and IgNF-B.
39. (Original) A method of detecting DNA or RNA encoding a

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transcriptional regulatory factor, comprising contacting a sample to be tested with a labeled DNA probe complementary to at least a portion the sequence of nucleic acid encoding a transcriptional regulatory factor; incubating the probe and the sample under hybridization conditions which permit the labeled probe to hybridize with complementary DNA or RNA sequences; removing unhybridized probe and analyzing the sample for hybridized probe.

40. (Original) A method of claim 39, for determination of expression of the factor, wherein the conditions of hybridization are sufficiently stringent such that the probe hybridizes only to nucleic acid sequences to which it is substantially complementary.
41. (Original) A method of claim 39, for the identification of a gene encoding a transcriptional regulatory factor, wherein the hybridization conditions are of a sufficiently relaxed stringency such that the probe will hybridize to DNA sequences which are not completely complementary.
42. (Original) Polyclonal or monoclonal antibody specifically reactive with a nuclear protein which binds, in a sequence specific manner, to a transcriptional regulatory DNA element of an immunoglobulin light chain gene, a transcriptional regulatory DNA element of an immunoglobulin heavy chain gene or both.
43. (Original) An immunoassay for detection of a transcriptional regulatory factor in a biological fluid, in which the antibody of claim 42 is used to detect the transcriptional regulatory factor.

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44. (Original) An immunoassay of claim 43, for detection of IgNF-B or NF- $\kappa$ B, wherein the antibody is specifically reactive with IgNF-B or NF- $\kappa$ B.
45. (Original) The recombinant phage \h3, ATCC 67629.
46. (Original) The recombinant phage OCT-2, ATCC 67630.
47. (Original) A method of identifying an agonist or an antagonist of gene transcription, comprising employing a gene encoding a transcriptional regulatory factor in an in vivo or in vitro assay to identify an agonist or antagonist of the factor or the gene encoding the factor.
48. (Original) An agonist or antagonist of the activity of a transcriptional regulatory factor of claim 1 or a gene encoding the factor.
49. (Original) DNA encoding the DNA binding domain of a transcriptional regulatory protein of claim 1.
50. (Original) A method of specifically stimulating gene transcription in a cell, comprising:
  - a) providing an expressible gene construct comprising DNA encoding the binding domain of a transcriptional regulatory factor linked to DNA encoding an activator of the RNA polymerase for the gene; and
  - b) introducing the construct into the cell.
51. (Original) A method of claim 50, wherein the DNA encodes the binding domain of IgNF-B or NF- $\kappa$ B.
52. (Original) A DNA construct comprising DNA encoding the

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binding domain of a transcriptional regulatory factor linked to DNA encoding an activator of the Rna polymerase of the gene.

53. (Original) A DNA construct of claim 52, wherein the DNA encodes the binding domain of IgNF-B or NF- $\kappa$ B.
54. (Original) A method of inducing expression of a gene, comprising the steps of:
  - a) preparing a DNA construct comprising:
    - i) a Kappa enhancer sequence or a portion of the Kappa enhancer sequence containing at least the sequence to which the factor NF- $\kappa$ B binds;
    - ii) a promoter; and
    - iii) a structural gene of interest.
  - b) transfecting a eukaryotic host cell with the DNA construct; and
  - c) stimulating the transfected cell with a substance which stimulates NF-B activation and binding to the enhancer sequence.
55. (Original) A method of claim 54, wherein the structural gene encodes a cytotoxic protein.
56. (Original) A method of claim 54, wherein the substance which stimulates NF-B is an activator of protein kinase C.
57. (Original) A method of altering expression in a cell of a gene whose transcriptional activity is altered by binding of NF- $\kappa$ B to the enhancer of said gene, comprising controlling dissociation of the NF- $\kappa$ B-I $\kappa$ B complex present in the cytoplasm of said cell.

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58. (Original) The method of reducing expression in a cell of a gene whose transcriptional activity is activated by binding of NF- $\kappa$ B to the enhancer of said gene, comprising preventing dissociation of NF- $\kappa$ B-I $\kappa$ B complex present in the cytoplasm of said cell.
59. (Original) A method of activating in a host cell an NF- $\kappa$ B precursor present in the cytoplasm of said host cell, the precursor comprising an NF- $\kappa$ B-I $\kappa$ B complex, comprising contacting the host cell with a substance which causes dissociation of the complex into I $\kappa$ B and translocation of said NF- $\kappa$ B into the nucleus of said cell.
60. (Original) A method of preventing activation in a host cell of an NF- $\kappa$ B precursor present in the cytoplasm of said host cell, the precursor comprising an NF- $\kappa$ B-I $\kappa$ B complex, comprising contacting the host cell with a substance which prevents dissociation of the complex into I $\kappa$ B and NF- $\kappa$ B.
61. (Original) A method of causing activation of an NF- $\kappa$ B precursor, present in the cytosol of a host cell, the NF- $\kappa$ B precursor being an NF- $\kappa$ B-I $\kappa$ B complex, comprising treating the cell with a substance which causes dissociation of the NF- $\kappa$ B complex, resulting in induction of DNA-binding activity and nuclear translocation of the NF- $\kappa$ B present in the complex.
62. (Original) A method of controlling expression of human immunodeficiency virus DNA in a host cell latently infected with human immunodeficiency virus DNA, comprising preventing binding of NF- $\kappa$ B to human immunodeficiency virus transcriptional control elements.

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63. (Original) A method of claim 62 wherein binding of NF- $\kappa$ B to immunodeficiency virus transcriptional control elements is prevented by inhibiting dissociation of an NF- $\kappa$ B-I $\kappa$ B complex present in the cytoplasm of said host cell into I $\kappa$ B and NF- $\kappa$ B.
64. (Original) Isolated NF- $\kappa$ B-I $\kappa$ B complex.
65. (Original) Isolated DNA encoding NF- $\kappa$ B-I $\kappa$ B complex.
66. (Original) A method of regulating NF- $\kappa$ B-mediated gene expression in a cell, comprising altering NF- $\kappa$ B activity in the cell.
67. (Original) A method of regulating transduction in a cell of an extracellular signal by NF- $\kappa$ B, comprising altering NF- $\kappa$ B activity in the cell.
68. (Original) A method of claim 67 wherein NF- $\kappa$ B activity is reduced.
69. (Original) A method of claim 67 wherein NF- $\kappa$ B is enhanced.
70. (Original) A method of regulating NF- $\kappa$ B-mediated expression of a selected gene in a cell, comprising introducing into the cell a substance which regulates NF- $\kappa$ B activity in the cell.
71. (Original) A method of positively regulating NF- $\kappa$ B-mediated gene expression in a cell, comprising:
  - a) introducing into the cell a gene construct comprising a gene of interest, a DNA sequence which is the binding site of NF- $\kappa$ B and a promoter for the gene; and

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b) maintaining the cell under conditions appropriate for expression of the gene.

72. (Original) A method of claim 71 wherein the binding site is represented by the following consensus sequence:

C C  
GGGRATYYAC  
T T

or equivalents thereof.

73. (Original) A method of claim 72 wherein the consensus sequence is present in the group consisting of: the Ig  $\kappa$  enhancer regulatory element, the SV40 enhancer regulatory element, the HIV long terminal repeat, a regulatory element of the MHC class I H2-K gene, a regulatory element of the IL-2 lymphokine gene, a regulatory element of the IL-2R gene, and a regulatory element of the interferon  $\beta$  PRDII gene.

74. (Original) A method of positively regulating the expression of a gene in a cell, the gene having a DNA sequence which is a binding site of NF- $\kappa$ B, said method comprising introducing an effective amount of NF- $\kappa$ B into the cell, under conditions appropriate for binding of NF- $\kappa$ B to the binding site.

75. (Original) A method of positively regulating in a cell the expression of a gene comprising a DNA sequence which is a binding site of NF- $\kappa$ B, comprising introducing into the cell a gene construct encoding NF- $\kappa$ B and maintaining the cell, under conditions appropriate for expression of the gene.

76. (Original) A method of positively regulating the expression

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of a gene in a cell, the gene having a DNA sequence encoding a binding site of NF- $\kappa$ B, said method comprising inducing NF- $\kappa$ B activity by introducing into the cell an NF- $\kappa$ B inducing substance.

77. (Original) A method of claim 76 wherein the NF- $\kappa$ B inducing substance is selected from the group consisting of lipopolysaccharide, cyclohexamide, phorbol esters, virus, and tumor necrosis factor  $\alpha$  phorbol myristate.
78. (Original) A method of negatively regulating the expression of a gene in a cell, the gene having a binding site of NF- $\kappa$ B, said method comprising introducing an inhibitor of NF- $\kappa$ B into the cell, under conditions appropriate for binding of the inhibitor NF- $\kappa$ B.
79. (Original) A method of claim 78 wherein the inhibitor of NF- $\kappa$ B is I- $\kappa$ B.
80. (Original) A method of negatively regulating the expression of a gene in a cell, the gene having a binding site of NF- $\kappa$ B, said method comprising introducing a gene construct encoding I- $\kappa$ B cell, under conditions appropriate for I- $\kappa$ B production and binding of I- $\kappa$ B to NF- $\kappa$ B.
81. (Original) A method of negatively regulating the expression of a gene in a cell, the gene having a binding site of NF- $\kappa$ B, said method comprising introducing into the cell a DNA sequence which is the binding site of NF- $\kappa$ B, under conditions appropriate for binding of the DNA sequence and NF- $\kappa$ B.
82. (Original) A method of claim 81 wherein the binding site is

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represented by the following consensus of:

C C

GGGRATYYAC,

T T

or equivalents thereof.

83. (Original) A method of claim 81 wherein the consensus sequence is present in the group consisting of: the Ig  $\kappa$  enhancer regulatory element, the SV40 enhancer regulatory element, the HIV long terminal repeat, a regulatory element of the MHC class I H2-K gene, a regulatory element of the IL-2 lymphokine gene, a regulatory element of the IL-2R gene, and a regulatory element of the interferon  $\beta$  PRDII gene.
84. (Original) A method of modifying the expression of at least one gene in a cell, the gene having an NF- $\kappa$ B binding site, said method comprising introducing into the cell a gene construct comprising DNA encoding a modified NF- $\kappa$ B molecule which binds selectively to the NF- $\kappa$ B binding site of said selected gene or genes, under conditions appropriate for expression of the encoded modified NF- $\kappa$ B and binding of the modified NF- $\kappa$ B to the NF- $\kappa$ B binding site of said gene or genes.
85. (Original) A method of negatively regulating the expression of a gene in a cell, the gene having a DNA sequence encoding a binding site of NF- $\kappa$ B, said method comprising introducing into the cell a gene construct, the construct comprising DNA encoding a modified NF- $\kappa$ B molecule which comprises a DNA binding domain and lacks a RNA polymerase activating domain.

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86. (Original) Isolated or recombinant I $\kappa$ B.
87. (Original) A composition comprising an NF- $\kappa$ B inhibitor.
88. (Original) A composition of claim 85 wherein the inhibitor is a peptide capable of binding NF- $\kappa$ B.
89. (New) A method for reducing expression in a human cell of a gene, the expression of which has been induced by an external influence that activates NF- $\kappa$ B to act as an intracellular messenger to transmit a signal that induces expression of the gene from the plasma membrane of the cell to the nucleus of the cell, which method comprises within the cell inhibiting transmission of the signal so as to thereby reduce expression of the gene in the cell.
90. (New) A method for reducing expression in a human cell of a gene, the expression of which has been induced by an external influence that activates NF- $\kappa$ B to act as an intracellular messenger to transmit a signal that induces expression of the gene in the cell, which method comprises within the cell inhibiting transmission of the signal so as to thereby reduce expression of the gene in the cell.

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**REMARKS**

Claims 1-88 were pending in the subject application. By this Amendment, applicants have canceled claim 31 and added new claims 89 and 90.

Support for new claims 89 and 90 may be found, *inter alia*, on page 8, lines 1-7; on page 27, lines 17-20; and on page 8, line 16 to page 9, line 9 of the subject application.

**Restriction Requirement**

In the March 28, 2006 Restriction Requirement, the Examiner required restriction to one of the following allegedly distinct inventions as follows:

- I. Claims 1-4, drawn to isolated nuclear proteins which bind to transcriptional regulatory DNA elements of immunoglobulin genes;
- I.
- II. Claims 5-6, drawn to isolated nuclear proteins which bind to DNA sequences upstream of both mouse heavy kappa light chain gene promoters and binds to mouse heavy chain gene enhancer;
- III. Claims 7-9, and 49 drawn to isolated nucleic acids encoding nuclear proteins which bind to transcriptional regulatory DNA elements of immunoglobulin genes;
- IV. Claim 10, drawn to isolated DNA encoding a structural gene for a nuclear protein which binds in a sequence specific manner to the kappa enhancer;
- V. Claims 11-12, drawn to isolated DNA which encodes a nuclear

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protein which binds to DNAs in the upstream region of both mouse heavy and kappa light chain gene promoters and binds to DNA sequences of mouse heavy chain gene enhancer;

VI. Claim 13, drawn to a cloned DNA sequence which encodes a protein which binds to TGGGGATTCCCCA and hybridizes to a 10kb RNA transcript from both B and non-B human cells;

VII. Claims 14-16, drawn to an assay for detection of binding of cellular nuclear protein to DNA;

VIII. Claims 17-23, drawn to a method of enhancing the transcription of a gene of interest whose transcription is regulated by a regulatory factor which binds DNA in the vicinity of a gene;

IX. Claims 24-27, drawn to lymphoid cells;

X. Claim 28, drawn to a method of screening for the expression of a sequence-specific binding protein by a recombinant expression vector;

XI. Claims 29-35, drawn to a method of identifying recombinant expression vectors;

XII. Claims 36-41, drawn to DNA probes and methods of detecting DNA or RNA;

XIII. Claims 42-44, drawn to polyclonal or monoclonal antibodies and an immunoassay;

XIV. Claim 45, drawn to phage lambda h3, ATCC 67629;

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XV. Claim 46, drawn to phage OCT-2, ATCC 67630;

XVI. Claim 47, drawn to a method of identifying an agonist of gene transcription;

XVII. Claims 48, and 87-88, drawn to an agonist or antagonist of nuclear proteins which bind to transcriptional regulatory DNA elements of immunoglobulin genes;

XVIII. Claims 50-53, drawn to a method of specifically stimulating gene transcription in a cell;

XIX. Claims 54-56, drawn to a method of inducing expression of a gene;

XX. Claims 57-61, drawn to a method of altering expression in a cell of a gene whose transcriptional activity is altered by binding of NK- $\kappa$ B to the enhancer of said gene;

XXI. Claims 62-63, drawn to a method of controlling expression of HIV DNA in a host cell;

XXII. Claim 64, drawn to an isolated NF- $\kappa$ B - I $\kappa$ B complex;

XXIII. Claim 65, drawn to isolated DNA encoding NF- $\kappa$ B - I $\kappa$ B complex;

XXIV. Claims 66-73, drawn to a method of regulating NF- $\kappa$ B mediated gene expression in a cell;

XXV. Claims 74-77, drawn to a method of positively regulating the expression of a gene in a cell;

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XXVI. Claims 78-83, drawn to a method of negatively regulating the expression of a gene in a cell;

XXVII. Claims 84-85, drawn to a method of modifying the expression of at least one gene in a cell, the gene having a NF- $\kappa$ B binding site; and

XXVIII. Claim 86, drawn to isolated or recombinant I $\kappa$ B.

**Applicants' reply**

In response, applicants hereby elect, with traverse, the Group which includes new claims 89 and 90, which appears to be Group XXIV. Applicants also respectfully request examination of at least new claims 89 and 90 if no other claims are rejoined upon consideration of applicants' reasons below for traverse of the March 28, 2006 restriction requirement.

Applicants respectfully traverse the March 28, 2006 restriction requirement because it is not in compliance with 35 U.S.C. §121 which permits restriction only if two or more independent and distinct inventions are claimed in one application. Under M.P.E.P. §803, the Examiner must examine the application on the merits, even though it includes claims to distinct inventions, if the search and examination of an application can be made without serious burden.

The purported inventions of Groups I-XXVIII are not independent. Under M.P.E.P. §802.01, "independent" means there is no disclosed relationship between the subjects disclosed. The inventions of the Groups all relate to a new transcription factor, NF- $\kappa$ B, which is common to all the claims. The Examiner's grouping of the claims merely separates specific examples of the use of applicants' new discovery into different groups. However,

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knowledge of NF- $\kappa$ B and its activity is common to all of the examples.

Furthermore, under M.P.E.P. § 803, the Examiner must examine the application on the merits if examination can be made without serious burden, even if the application would include claims to distinct or independent inventions. That is, there are two criteria for a proper requirement for restriction: 1) the invention must be independent and distinct, **and** 2) there must be a serious burden on the Examiner if restriction is not required.

Applicants respectfully submit that there would not be a serious burden on the Examiner if restriction is not required because a search of the prior art relevant to NF- $\kappa$ B would necessarily uncover any existing prior art relevant to each of the purported Groups. Since there is no burden on the Examiner to examine the Groups together in the subject application, the Examiner must examine the entire application on the merits.

In view of the foregoing, applicants maintains that restriction is not proper under 35 U.S.C. § 121 and respectfully requests that the Examiner reconsider and withdraw the requirement for restriction.

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**Supplemental Information Disclosure Statement**

In accordance with their duty of disclosure under 37 C.F.R. §1.555, Applicants direct the Examiner's attention to the following disclosures, which are listed on Form PTO-1449 (**Exhibit A**). Copies of all of the references listed have been submitted in connection with U.S. Patent No. 6,410,516 and its in reexamination proceedings (*Ex Parte Reexamination Control Nos. 90/007,503, filed April 4, 2005, and 90/007,828, filed December 2, 2005*). The subject application claims benefit of the filing date of U.S. Patent No. 6,410,561 under 35 U.S.C. §120. Accordingly, copies of items 1-375 are not attached to this Supplemental Information Disclosure Statement but are readily available to the Examiner and to the public from the file history of U.S. Patent No. 6,410,516.

1. U.S. Patent No. 5,804,374, issued September 8, 1998, Baltimore et al.;
2. U.S. Patent No. 6,150,090, issued November 21, 2000, Baltimore et al.;
3. File history of U.S. Serial No. 06/817,441, filed January 9, 1986;
4. File history of U.S. Serial No. 06/946,365, filed December 24, 1986;
5. File history of U.S. Serial No. 07/155,207, filed February 12, 1988;
6. File history of U.S. Serial No. 07/162,680, filed March 1, 1988;

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7. File history of U.S. Serial No. 07/280,173, filed December 5, 1988;
8. File history of U.S. Serial No. 07/318,901, filed March 3, 1989;
9. File history of U.S. Serial No. 07/341,436, filed April 21, 1989;
10. File history of U.S. Serial No. 07/791,898, filed November 13, 1991 Abandoned;
11. File history of U.S. Serial No. 08/418,266, filed April 6, 1995;
12. File history of U.S. Serial No. 08/463,397, filed June 5, 1995;
13. File history of U.S. Serial No. 08/464,364, filed June 5, 1995;
14. File history of U.S. Serial No. 08/959,160 filed October 28, 1997;
15. File history of U.S. Serial No. 10/037,341, filed January 4, 2002;
16. File history of U.S. Serial No. 10/037,415 filed January 4, 2002;
17. WO 92/20795, 26 Nov. 1992, PCT/US92/04073, filed 14 May 1992;

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18. Alroy, I. et al., "Transcriptional Repression of the Interleukin-2 Gene By Vitamin D3: Direct Inhibition of NFATp/AP-1 Complex Formation by a Nuclear Hormone Receptor", *Molecular and Cellular Biology* (1995) 15:5789-5799;
19. Aoki, N., "Patenting Biological Pathways", *Boston Globe* (2002) pg. 1 and 3;
20. Auphan, N. et al., "Immunosuppression by Glucocorticoids: Inhibition of NF- $\kappa$ B Activity Through Induction of I $\kappa$ B Synthesis", *Science* (1995) 270:286-290;
21. Baeuerle, P., "NF- $\kappa$ B: Ten Years After", *Cell*, (1996) 87:13-20;
22. Baeuerle, P.A. "NF- $\kappa$ B as a Frequent Target For Immunosuppressive and Anti-Inflammatory Molecules", *Advances in Immunology* (1997) 55:111-137;
23. Baeuerle, P.A. et al., "Phorbol-ester-induced Activation Of the NF- $\kappa$ B Transcriptional Factor Involves Dissociation of an Apparently Cytoplasmic NF- $\kappa$ B/Inhibitor Complex", *Cold Spring Harbor Symposia on Quantitative Biology* (1988) Vol. LIII pgs 789-798;
24. Baeuerle, P.A., "Activation of NF- $\kappa$ B: A transcription factor controlling expression of the immunoglobuli  $\kappa$  light-chain gene and of HIV," *The Control of Human Retrovirus Gene Expression*, Banbury Conference, Cold Spring Harbor, NY (1988), pp.:217-226;
25. Baeuerle, P.A., "The Inducible Transcription Activator

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 25 of 103 of September 28, 2006 Amendment

NF-κB: Regulation by Distinct Protein Subunits", Biochimica Biophysica. Acta. (1991) 1072:63-80;

26. Baldwin Jr., A.S., "The NF-κB and IκB Proteins: New Discoveries and Insights", Annu. Rev. Immunol. (1996) 14:649-81;
27. Baldwin Jr., A.S., "The Transcription Factor NF-κB and Human Disease", The Journal of Clinical Investigation (2001) 103:3-5;
28. Baltimore, D., "Gene Therapy: Intracellular Immunization", Nature (1988) 335:395-396;
29. Ballard, D.W. et al. "HTLV-1 Tax induces cellular proteins that activate the κB element in the IL-2 receptor a gene," Science (1988), 241:1652-1657;
30. Banjeri, J. et al., "A lymphocyte-specific cellular enhancer is located downstream of the joining region in immunoglobulin heavy chain genes," Cell (1983), 33:729-740;
31. Banerji, S. et al., "The Immunosuppressant FK-506 Specifically Inhibits Mitogen-Induced Activation of the Interleukin-2 Promoter and the Isolated Enhancer Elements NFIL-2A and NF-AT1", Molecular and Cellular Biology (1991) 11:4074-4087;
32. Beg, A.A. et al., " Tumor Necrosis Factor and Interleukin-1 Lead to Phosphorylation and Loss of IκB $\alpha$ : a Mechanism for NF-κB Activation", Molecular and Cellular Biology (1993) 13:3301-3310;

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 26 of 103 of September 28, 2006 Amendment

33. Beg, A.A. et al., "Embryonic Lethality and Liver Degeneration In Mice Lacking The RelA Component of NF- $\kappa$ B", Nature (1995) 376:167-170;
34. Bergman, Y. et al., "Two regulatory elements for immunoglobulin  $\kappa$  light chain gene expression," Proc. Natl. Acad. Sci. USA, (1984), 81:7041-7045;
35. Bergmann, M. et al., "Glucocorticoid Inhibition of Granulocyte Macrophage-Colony-Stimulating Factor From T Cells Is Independent of Control by Nuclear Factor- $\kappa$ B and Conserved Lymphokine Element O", American Journal of Respiratory Cell and Molecular Biology (2004) 30:555-563;
36. Bergmann, M. et al., "Nuclear Factor- $\kappa$ B Does Not Mediate The Inhibitory Effects of Dexamethasone On Granulocyte-Macrophage Colony-Stimulating Factor Expression", Immunology (2004) 111:430-434;
37. Beutler, B. et al., "Control of Cachectin (Tumor Necrosis Factor) Synthesis: Mechanisms of Endotoxin Resistance", Science (1986) 232:977-980;
38. Blanar, M.A. et al., "A Gamma-Interferon-Induced Factor That Binds The Interferon Response Sequence Of the MHC Class I Gene, H-2K<sup>b</sup>", The EMBO Journal (1989) 8:1139-1144;
39. Blanar, M.A. et al., "Nf- $\kappa$ B binds within a region required for B-Cell-specific expression of the major histocompatibility complex class II gene ead," Mol. & Cell. Biol. 9(2):844-846;
40. Blanco-Colio, L.M. et al., "Red Wine Intake Prevents

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 27 of 103 of September 28, 2006 Amendment

Nuclear Factor- $\kappa$ B Activation In Peripheral Blood Mononuclear Cells of Healthy Volunteers During Postprandial Lipemia", Circulation (2000) 102:1020-1026;

41. Bochkov, V.N. et al., "Oxidized Phospholipids Stimulate Tissue Factor Expression In Human Endothelial Cells Via Activation of ERK/EGR-1 and Ca<sup>++</sup>/NFAT", Blood (2002) 99:199-206;
42. Bohnlein, E. et al., "The same inducible nuclear proteins regulates mitogen activation of both the interleukin-2 receptor-alpha gene and type 1 HIV", Cell (1988), 53:827-836;
43. Bressler et al., Journal of Virology (1993) 67:288-293, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
44. Brostjan, C. et al., "Glucocorticoid-Mediated Repression of Nf $\kappa$ B Activity in Endothelial Cells Does Not Involve Induction of I $\kappa$ B $\alpha$  Synthesis", The Journal of Biological Chemistry (1996) 271:19612-19616;
45. Caldenhoven, E. et al., "Negative Cross-Talk Between RelA and the Glucocorticoid Receptor: A Possible Mechanism for the Antiinflammatory Action of Glucocorticoids", Mol. ENDO (1995) 9:401-412;
46. Callejas, N.A. et al., "Absence of Nuclear Factor  $\kappa$ B Inhibition by NSAIDs in Hepatocytes", Hepatology (2002) 35:341-348;
47. Castrillo, A. et al., "Inhibition of I $\kappa$ B Kinase and I $\kappa$ B

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 28 of 103 of September 28, 2006 Amendment

Phosphorylation by 15-Deoxy- $\Delta^{12,14}$ -Prostaglandin J<sub>2</sub> in Activated Murine Macrophages", Molecular And Cellular Biology (2000) 20:1692-1698;

48. Cenci, S. et al., "Estrogen Deficiency Induces Bone Loss By Enhancing T-Cell Production of TNF- $\alpha$ ", The Journal of Clinical Investigation (2000) 106:1229-1237;
49. Church, G. M. Et al., "Cell-type-specific contacts to immunoglobulin enhancers in nuclei," Nature (1985), 313:798-801;
50. Cogswell, P.C. et al., "Promoter Of The Human NF- $\kappa$ B p50/p105 Gene Regulation by NF- $\kappa$ B Subunits and by c-RELL", The Journal of Immunology (1993) 150:2794-2804;
51. Cohen, J., Nature (2002) 420:885-891, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
52. Collart, M.A. et al., "Modulations of Functional Activity In Differentiated Macrophages Are Accompanied By Early And Transient Increase or Decrease In c-FOS Gene Transcription", The Journal of Immunology (1987) 139:949-955;
53. Collart, M.A., "Regulation of Tumor Necrosis Factor Alpha Transcription in Macrophages: Involvement of Four  $\kappa$ B-Like Motifs and of Constitutive and Inducible Forms of NF- $\kappa$ B", Molecular & Cellular Biology (1990) 10:1498-1506;
54. DeBosscher, K. et al., "Glucocorticoid-Mediated Repression of Nuclear Factor- $\kappa$ B-Dependent Transcription Involves Direct Interference With Transactivation", Proc. Natl.

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 29 of 103 of September 28, 2006 Amendment

Acad. Sci. USA (1997) 94:13504-13509;

55. Din, FVN, "Evidence For Colorectal Cancer Cell Specificity Of Aspirin Effects On NfkB Signalling and Apoptosis", British Journal of Cancer (2004) 91:381-388;
56. Dofferhoff et al., Scand. J. Infect. (1991) 23:739-754, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
57. Epstein, F.H., The New England Journal of Medicine (1997) 336:1066-1071, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
58. Evans and Pollack, The Journal of Infectious Diseases (1993) 167:1336-43, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
59. Fan, Chen-Ming, "A DNA-Binding Protein Containing Two Widely Separated Zinc Finger Motifs That Recognize The Same DNA Sequence", Genes & Development (1990) 4:29-42;
60. Fan, Chen-Ming, "Generation of p50 Subunit of NF- $\kappa$ B by Processing of p105 Through an ATP-Dependent Pathway", Nature (1991) 354:395-398;
61. Fan, Chen-Ming, "Two Different Virus-Inducible Elements Are Required For Human  $\beta$ -Interferon Gene Regulation", The EMBO Journal (1989) 8:101-110;
62. Fletcher, C., et al., "Purification and characterization of OTF-1, a transcription factor regulating cell cycle expression of a human histone H2b gene," Cell (1987),

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 30 of 103 of September 28, 2006 Amendment

51:773-781;

63. Foster, J. et al., "An immunoglobulin promoter displays cell-type specificity independently of the enhancer," *Nature* (1985), 315:423-425;
64. Frantz, B. et al., "Calcineurin Acts In Synergy With PMA To Inactivate I $\kappa$ B/MAD3 an Inhibitor of NF- $\kappa$ B", *The EMBO Journal* (1994) 13:881-870;
65. Fried, M. And Crothers, D.M., "Equilibria and kinetics of lac repressor-operator interactions by polyacrylamide gel electrophoresis," *Nucleic Acids Research*, (1981), 9(23):6505-6524;
66. Galdiero et al., *Microbiology* (2001) 147:2697-2704, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
67. Garner, M.M. and Revzin, A., "A gel electrophoresis method for quantifying the binding of proteins to specific DNA regions; application to components of the *Escherichia coli* lactose operon regulatory system," *Nucleic Acids Research* (1981), 9(13):3047-3060;
68. Gerster, T. Et al., "Cell type-specificity elements of the immunoglobulin heavy chain gene enhancer," *EMBO Journal* (1987) 6(5):1323-1330;
69. Giffin, M.J. et al., "Structure of NFAT1 Bound As A Dimer To The HIV-1 LTR  $\kappa$ B Element", *Nature Structural Biology* (2003) 10:800-806;

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 31 of 103 of September 28, 2006 Amendment

70. Goldfeld, A.E., "Coordinate Viral Induction Of Tumor Necrosis Factor  $\alpha$  and Interferon  $\beta$  In Human B cells and Monocytes", Proc. Natl. Acad. Sci. USA (1989) 86:1490-1494;
71. Goldfeld, A.E., "Human Tumor Necrosis Factor  $\alpha$  Gene Regulation By Virus and Lipopolysaccharide", Proc. Natl. Acad. Sci. USA (1990) 87:9769-9773;
72. Goodbourn, S. et al., "Human  $\beta$ -interferon gene expression is regulated by an inducible enhancer element," Cell (1985), 41:509-520;
73. Goodman & Gilman's The Pharmacological Basis of Therapeutics, Ninth Edition, Chapter 27, R.R. Donnelley and Sons Co., (1996) pg 625-631 including Table A-II-1 pg 1780 and pg 1712;
74. Goodman & Gilman's The Pharmacological Basis of Therapeutics, Ninth Edition, Chapter 27, R.R. Donnelley and Sons Co., (1996) pg 633-635 including pg 1783;
75. Gosh, S. And Baltimore, D., "Activation in vitro of NF- $\kappa$ B by phosphorylation of its inhibitor I $\kappa$ B," Nature, (1990), 344(6267):678-682;
76. Grilli, M. et al., "NF- $\kappa$ B and Rel: Participants In A Multiform Transcriptional Regulatory System", International Review of Cytology (1993) 143:1-62;
77. Grilli, M. et al., "Tumor Necrosis Factor  $\alpha$  Mediates A T Cell Receptor-Independent Induction Of The Gene Regulatory Factor NF- $\kappa$ B In T Lymphocytes", Molecular Immunology (1993) 30:1287-1294;

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 32 of 103 of September 28, 2006 Amendment

78. Grosschedi, R. And Baltimore D., "Cell-type specificity of immunoglobulin gene expression is regulated by at least three DNA sequence elements," *Cell* (1985), 41:885-897;
79. Hämäläinen, M. et al., "Calcineurin Inhibitors, Cyclosporin A and Tacrolimus Inhibit Expression of Inducible Nitric Oxide Synthase In Colon Epithelial And Macrophage Cell Lines", *European Journal of Pharmacology* (2002) 448:239-244;
80. Han, C.W. et al., "Glucocorticoid-Mediated Repression of Inflammatory Cytokine Production In Fibroblast-Like Rheumatoid Synoviocytes Is Independent of Nuclear Factor- $\kappa$ B Activation Induced By Tumor Necrosis Factor  $\alpha$ ", *Rheumatology* (2001) 40:267-273;
81. Ho, S. et al., "The Mechanism of Action of Cyclosporin A and FK506", *Clinical Immunology and Immunopathology* (1996) 80:S40-S45;
82. Hofmann, T.G., "The Promoter Context Determines Mutual Repression or Synergism Between NF- $\kappa$ B and the Glucocorticoid Receptor", *Biol. Chem.* (2002) 383:1947-1951;
83. Hoffman et al., *Science* (2002) 298:1241-1245, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
84. Hogan P. Et al., "Transcriptional Regulation by Calcium, Calcineurin, and NFAT", *Genes & Development* (2003) 17:2205-2232;
85. Hölschermann, H. et al., "Opposite Regulation of Tissue

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 33 of 103 of September 28, 2006 Amendment

Factor Expression by Calcineurin in Monocytes and Endothelial Cells", The Journal of Immunology (2001) 166:7112-7120;

86. Horwitz, B. et al., "Failure of Lymphopoiesis After Adoptive Transfer of NF- $\kappa$ B-Deficient Fetal Liver Cells", Immunity (1997) 6:765-772;
87. Hurley et al., Antimicrobial Agents and Chemotherapy (1991) 35:2388-2394, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
88. Ito, C.Y. et al., "Three NF- $\kappa$ B Sites in the I $\kappa$ B- $\alpha$  Promoter Are Required for Induction of Gene Expression by TNF $\alpha$ ", Nucleic Acids Research (1994) 22:3787-3792;
89. Janssen-Heininger, et al., "Recent Advances Towards Understanding Redox Mechanisms In the Activation of Nuclear Factor  $\kappa$ B", Free Radical Biology & Medicine (2000) 28:1317-1327;
90. Johnston et al., "Present status and future prospects for HIV therapies," Science (1993), 260:1286-1293;
91. Karin, M. et al., "Activation of a heterologous promoter in response to dexamethasone and cadmium by metallothionein gene 5' flanking DNA," Cell (1984), 36:371-379;
92. Kawakami, K., et al., "Identification and purification of a human immunoglobulin-enhancer-binding protein (NF- $\kappa$ B) that activates transcription from a human immunodeficiency virus type 1 promoter in vitro," Proc. Natl. Acad. Sci. USA, (1988), 85:4700-4704;

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 34 of 103 of September 28, 2006 Amendment

93. Keller, A.D., "Identification of an Inducible Factor That Binds To A Positive Regulatory Element of The Human B-Interferon Gene", Proc. Natl. Acad. Sci. USA (1988) 85:3309-3313;
94. Kerr, L.D. et al., "The Rel-Associated pp40 Protein Prevents DNA Binding of Rel and NF- $\kappa$ B: Relationship With I $\kappa$ B $\beta$  and Regulation by Phosphorylation", Genes & Development (1991) 5:1464-1476;
95. Kim, Hyoung-Pyo, "The Basis For TCR-Mediated Regulation of the IL-2 Receptor  $\alpha$  Chain Gene: Role of Widely Separated Regulatory Elements", The EMBO Journal (2002) 21:3051-3059;
96. Kinoshita, S. et al., "The T Cell Activation Factor NF-ATc Positively Regulates HIV-1 Replication and Gene Expression in T Cells", Immunity (1997) 6:235-244;
97. Ko, H.S. et al., "A human protein specific for the immunoglobulin octamer DNA motif contains a functional homeobos domain," Cell (1988), 55:135-144;
98. Kopp, E., "Inhibition of NF- $\kappa$ B by Sodium Salicylate and Aspirin", Science, (1994) 265:956-959;
99. Krönke, M. et al., "Cyclosporin A Inhibits T-cell Growth Factor Gene Expression At the Level of mRNA Transcription", Proc. Natl. Acad. Sci. USA (1984) 81:5214-5218;
100. Landolfi, N.F. et al., "Interaction of cell-type-specific nuclear proteins with immunoglobulin V $H$  promoter region sequences," Nature (1986), 323:548-551;

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 35 of 103 of September 28, 2006 Amendment

101. Leeson and Morrison, Shock (1994) 2:235-245, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
102. Leonard et al., "Interleukin 2 receptor gene expression in normal human T lymphocytes", Proc. Natl. Acad. Sci. USA (1985), 82:6281-6285;
103. Lenardo, J.J. et al., "NF- $\kappa$ B protein purification from bovine spleen: Nucleotide stimulation and binding site specificity," Prod. Natl. Acad. Sci. USA, (1988), 85:8825-8829;
104. Lenardo, M.J. et al., "The Involvement of NF- $\kappa$ B in  $\beta$ -Interferon Gene Regulation Reveals Its Role as Widely Inducible Mediator of Signal Transduction", Cell (1989) 57:287-294;
105. Lenardo, M.J., "NF- $\kappa$ B-a Paradigm For Inducible and Tissue-Specific Gene Control", Draft 3/28/89;
106. Lepper et al., Intensive Care Med. (2002) 28:824-833, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
107. Leung, K. And Nable, G.J., "HTLV-1transactivator induces interleukin-2 receptor expression through an NF- $\kappa$ B-like factor", Nature (1988), 333:776-778;
108. Liou, Hsiou-Chi, "Regulation of the NF- $\kappa$ B/rel Transcription Factor And I $\kappa$ B Inhibitor System", Current Opinion in Cell Biology (1993) 5:477-487;

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 36 of 103 of September 28, 2006 Amendment

109. Locksley, R. et al., "The TNF and TNF Receptor Superfamilies: Integrating Mammalian Biology", *Cell* (2001) 104:467-501;
110. Logeat et al., *The EMBO Journal* (1991) 10:1827-1832, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
111. LyB, G. et al., "The Anti-Inflammatory Sesquiterpene Lactone Helenalin Inhibits the Transcription Factor NF- $\kappa$ B by Directly Targeting p65", *The Journal of Biological Chemistry* (1998) 273:33508-33516;
112. Mason, J.O. et al., "Transcription cell type specificity is conferred by an immunoglobulin V<sub>H</sub> gene promoter that includes a functional consensus sequence," *Cell* (1985), 41:479-487;
113. Matsuda, S., "Mechanisms of Action of Cyclosporine", *Immunopharmacology* (2000) 47:119-125;
114. Mauxion, F., "Alteration of a Single Nucleotide Allows Efficient Binding of H2TF1/KBF1 To The Immunoglobulin K Enhancer B Motif", *Molecular & Cellular Biology* (1989) 9:3548-3552;
115. Mauxion, F. et al., "Comparison of Constitutive and Inducible Transcriptional Enhancement Mediated by  $\kappa$ B-related Sequences: Modulation of Activity in B Cells by Human T-Cell Leukemia Virus Type I tax Gene", *Proc. Natl. Acad. Sci. USA* (1991) 88:2141-2145;
116. McCaffrey, P.G. et al., "Cyclosporin A Sensitivity Of The

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 37 of 103 of September 28, 2006 Amendment

NF- $\kappa$ B Site of the IL2R $\alpha$  Promoter In Untransformed Murine T Cells", Nucleic Acids Research (1994) 22:2134-2142;

117. Mercola, M. et al., "Transcriptional enhancer elements in the mouse immunoglobulin heavy chain locus," Science, (1983) 221:663-665;
118. Mercola, M. et al., "Immunoglobulin heavy-chain enhancer requires one or more tissue-specific factors," Science (1985), 227:266-270;
119. Mukaida, N. et al., "Novel Mechanism of Glucocorticoid-Mediated Gene Repression", The Journal of Biological Chemistry (1994) 969:13289-13295;
120. Mustafa et al., The Journal of Infectious Diseases (1989) 160:891-895, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
121. Nagpal, S., "Vitamin D Analogs: Mechanism of Action and Therapeutic Applications", Current Medicinal Chemistry (2001) 8:1661-1679;
122. Nelsen, B., "Regulation of Immunoglobulin Gene Transcription", International Review of Cytology, (1992) 133:121-149;
123. Nelson, K.J., et al., "Inducible transcription of the unarranged  $\kappa$  constant region locus is a common feature of pre-B cells and does not require DNA or protein synthesis," Proc. Natl. Acad. Sci. USA (1985) 82:5305-5309;
124. Nitsche et al., Arch Surg. (1996) 131:192-199, Document

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 38 of 103 of September 28, 2006 Amendment

201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

125. Park, Su-Kil, et al., "Dexamethasone Regulates AP-1 to Repress TNF- $\alpha$  Induced MCP-1 Production in Human Glomerular Endothelial Cells", *Nephrology Dial. Transplant.* (2004) 19:312-319;
126. Pendurthi, U.R. et al., "Resveratrol, a Polyphenolic Compound Found in Wine, Inhibits Tissue Factor Expression In Vascular Cells A Possible Mechanism for the Cardiovascular Benefits Associated With Moderate Consumption of Wine", *Arterioscler Thromb Vasc Biol.* (1999) 19:419-426;
127. Perez-G, M. et al., "Aspirin and Salicylates Inhibit the IL-4- and IL-13-Induced Activation of STAT6<sup>1</sup>", *The Journal of Immunology* (2002) 168:1428-1434;
128. Physicians' Desk Reference 24<sup>th</sup> ed. 1970, pgs. Cover, title page, Generic and Chemical Index Section 3, pg 305, 307, 309, 312, 326-328, Product Information 638-639, 809, 880-881, 1167, 1210-1211, 1309-1310, 1323, 1379-1380, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
129. Picard, D. And Schaffner, W., "A lymphocyte-specific enhancer in the mouse immunoglobulin  $\kappa$  gene," *Nature* (1984), 307:80-82;
130. Pruett, S.B. et al., "Characterization of Glucocorticoid Receptor Translocation, Cytoplasmic I $\kappa$ B, Nuclear Nf $\kappa$ B, and Activation of Nf $\kappa$ B in T Lymphocytes Exposed To Stress-Inducible Concentrations of Corticosterone In Vivo", *International Immunopharmacology* (2003) 3:1-16;

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 39 of 103 of September 28, 2006 Amendment

131. Queen, C. And Baltimore, D., "Immunoglobulin Gene Transcription Is Activated by downstream sequence elements," *Cell* (1983), 33:741-748;
132. Queen, C. And Stafford, J., "Fine mapping of an immunoglobulin gene activator," *Mol. Cel. Biol.* (1984), 4 (6):1042-1049;
133. Ray, A., "Physical Association And Functional Antagonism Between The p65 Subunit of Transcription Factor NF- $\kappa$ B and The Glucocorticoid Receptor", *Proc. Natl. Acad. Sci. USA* (1994) 91:752-756;
134. Rengarajan, J. et al., "Interferon Regulatory Factor 4 (IRF4) Interacts with NFATc2 to Modulate Interleukin 4 Gene Expression", *J. Exp. Med.* (2002) 195:1003-1012;
135. Ruben, S. et al., "Cellular transcription Factors and Regulation of IL-2 receptor gene expression by HTLV-1 tax gene product", *Science* (1988), 241:89-92;
136. Rupec, R.A. et al., "Structural Analysis, Expression, and Chromosomal Localization of the Mouse ikba Gene", *Immunogenetics* (1999) 49:395-403;
137. Ryu, Y.S. et al., "Acetaminophen Inhibits iNOS Gene Expression in RAW 264.7 Macrophages: Differential Regulation of NF- $\kappa$ B by Acetaminophen and Salicylates", *Biochemical and Biophysical Research Communications* (2000) 272:758-764;
138. Sadikot, R. T. et al., "High-Dose Dexamethasone Accentuates

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 40 of 103 of September 28, 2006 Amendment

Nuclear Factor- $\kappa$ B Activation in Endotoxin-Treated Mice",  
Am. J. Respir. Crit. Care Med. (2001) 164:873-878;

139. Sassone-Corsi, P. et al., "A trans-acting factor is responsible for the simian virus 40 enhancer activity in vitro," Nature (1985), 313:458-463;
140. Scheidereit, C. Et al., "Identification and purification of a human lymphoid-specific octamer-binding protein (OTF-2) that activates transcription of an immunoglobulin promoter in vitro," Cell (1987) 51:783-793;
141. Scheinman, R. et al., "Characterization of Mechanisms Involved In Transrepression of NF- $\kappa$ B by Activated Glucocorticoid Receptors", Molecular and Cellular Biology (1995) 15:943-953 ;
142. Fig. 7 and Fig. 8 of Scheinman, et al., "Characterization of Mechanisms Involved In Transrepression of NF- $\kappa$ B by Activated Glucocorticoid Receptors", Molecular and Cellular Biology (1995) 15:949-950;
143. Scheinman, R.I. et al., "Role of Transcriptional Activation of I $\kappa$ B $\alpha$  in Mediation of Immunosuppression by Glucocorticoids", Science (1995) 270:283-286;
144. Schmitz, M.L. et al., "Proteins Controlling The Nuclear uptake of NF- $\kappa$ B, Rel and Dorsal", Trends in Cell Biology (1991) 1:130-137;
145. Schreck, R. and Baeuerle, P., "A Role for Oxygen Radicals As Second Messengers", Trends In Cell Biology, Forum (1991) 1:39-42;

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 41 of 103 of September 28, 2006 Amendment

146. Schreiber, S.L., "The Mechanism of Action of Cyclosporin A and FK506" *Immunology Today* (1992) 13:136-142;
147. Shenep and Mogan, *The Journal of Infectious Diseases* (1984) 150:380-388, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
148. Sica, A. et al., "Interaction of NF- $\kappa$ B and NFAT With the Interferon- $\gamma$  Promoter", *The Journal of Biological Chemistry* (1997) 272:30412-30420;
149. Singh, H. et al., "A nuclear factor that binds to a conserved sequence motif in transcriptional control elements of immunoglobulin genes," *Nature* (1986), 319:154-158;
150. Stark, L.A. et al., "Aspirin-Induced Activation of the NF- $\kappa$ B Signaling Pathway: A Novel Mechanism For Aspirin-Mediated Apoptosis In Colon Cancer Cells<sup>1</sup>", *The FASEB Journal* (2001) 15:1273-1275;
151. Staudt, L.M., et al., "A lymphoid-specific protein binding to the octamer motif of immunoglobulin genes," *Nature* (1986), 323:640-643;
152. Staudt, L. et al., "Cloning of a lymphoid-specific cDNA encoding a protein binding the regulatory octamer DNA motif," *Science* (1988), 241:577-580;
153. Strauss, F. And Varshavsky, A., "A protein binds to a satellite DNA repeat at three specific sites that would be brought into mutually proximity by DNA folding in the

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
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nucleosome," Cell (1984), 37:889-901;

154. (2004) Surgeon General's Report including the following: Abbreviations and Acronyms; Acknowledgments ix-xxvi; Appendix A; Appendix B; Appendix C; Chapter 1: key Messages; Chapter 2: Key Messages; Chapter 3 Diseases of Bone; Chapter 4: Key Messages; Chapter 5: Key Messages; Chapter 6: Key Messages; Chapter 7: Key Messages; Chapter 8: Key Messages; Chapter 9: Key Messages; Chapter 10: Key Messages; Chapter 11: Key Messages; Chapter 12: Key Messages; Chapter 13: A Vision for the future: a framework for action to promote bone health; United States Department of Health & Human Services (2004); Index; Message from Tommy G. Thompson; Part Five; Part Four; Part One; Part Six; Part Three; Part Two; Preface; Bone Health and Osteoporosis A Report of the Surgeon General, in Civil Case 02 CV 11280 RWZ;
155. Taber's Cyclopedic Medical Dictionary 16<sup>th</sup> Ed. (1989), pp. 1120, Document 198-9, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
156. Takeuchi, A. et al., "Nuclear Factor of Activated T Cells (NFAT) As a Molecular Target For 1 $\alpha$ ,25-Dihydroxyvitamin D<sub>3</sub>-Mediated Effects", The Journal of Immunology (1998) 160:209-218;
157. Ting, J. Pan-Yun, "Regulation of MHC Gene Expression", Current Opinion in Immunology (1993) 5:8-16;
158. Ting and Endy, Science (2002) 298:1189-1190, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

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159. Traber, K.E. et al., "Anti-Rheumatic Compound Aurothioglucose Inhibits Tumor Necrosis Factor- $\alpha$ -Induced HIV-1 Replication in Latently Infected OM10.1 and Ach2 Cells", International Immunology (1999) 11:143-150;
160. Triesman R., "Transient accumulation of c-fos RNA following serum stimulation requires a conserved 5' element and c-fos 3' sequences", Cell (1985), 42:889-902;
161. Wadsworth, T.L., "Effects of the Wine Polyphenolics Quercetin and Resveratrol on Pro-Inflammatory Cytokine Expression in RAW 264.7 Macrophages", Biochemical Pharmacology (1999) 57:941-949;
162. Wahl, C. et al., "Sulfasalazine: A Potent and Specific Inhibitor of Nuclear Factor Kappa B", J. Clin. Invest. (1998) 101:1163-1174;
163. Wall, R. et al., "A labile inhibitor blocks immunoglobulin  $\kappa$ -light-chain-gne transcription in a pre-B leukemic cell line," Proc. Natl. Acad. Sci. USA, (1986), 83:295-298;
164. Wang, W. et al., "A NF- $\kappa$ B/c-myc-Dependent Survival Pathway Is Targeted by Corticosteroids In Immature Thymocytes<sup>1</sup>", The Journal of Immunology (1999) 162:314-322;
165. Wang, W. et al., "Pentoxifylline Inhibits Ig  $\kappa$  Gene Transcription And Rearrangements in Pre-B Cells<sup>1</sup>", The Journal of Immunology (1998) 160:1789-1795;
166. Weissmann, G. et al., "Non-Prostaglandin Effects of Aspirin III and Salicylate: Inhibition of Integrin-Dependent Human Neutrophil Aggregation And  $\kappa$ B (P105)- Knockout Mice",

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Eicosanoids and Other Bioactive Lipids in Cancer, Inflammation, and Radiation Injury 5 (2002) pgs 571-577;

167. Wirth T. And Baltimore D., "Nuclear factor NF- $\kappa$ B can interact functionally with its cognate binding site to provide lymphoid-specific promoter function," The EMBO Journal, (1988), 7(10):3109-3113;
168. Wu et al., "Purification of the human immunodeficiency virus type 1 enhancer and TAR binding proteins EBP-1 and UBP-1, EMBO (1988), 7:2117-2129;
169. Xigris drotrecogin alfa (activated) 2002-2004, EX 0579 0001-EX 0579 0049, in Civil Case 02 CV 11280 RWZ;
170. Yamamoto, Y. , "Therapeutic Potential of Inhibition of the NF- $\kappa$ B Pathway In The Treatment of Inflammation and Cancer", The Journal of Clinical Investigation (2001) 107:135-142;
171. Yamamoto, Y. et al., "Sulindac Inhibits Activation of the NF- $\kappa$ B Pathway", The Journal of Biological Chemistry (1999) 274:27307-27314;
172. Yan, F., "Aminosalicylic Acid Inhibits I $\kappa$ B Kinase  $\alpha$  Phosphorylation of I $\kappa$ B $\alpha$  in Mouse Intestinal Epithelial Cells", The Journal of Biological Chemistry (1999) 274:36631-36635;
173. Yin, Min-Jean et al., "The Anti-Inflammatory Agents Aspirin And Salicylate Inhibit The Activity of I $\kappa$ B Kinase- $\beta$ ", Nature (1998) 396:77-80; .
174. Zinn, K. et al., "Identification of Two Distinct Regulatory

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Regions Adjacent to the Human  $\beta$ -Interferon Gene", Cell (1983) 34:865-879;

175. February 11, 1983 Grant Application by Maniatis, Thomas Peter, NIH IEN Grant Proposal 1983-1988;
176. February 23, 1986 Grant Application by Maniatis, Thomas Peter, NIH AI20642 Interferon 1986-1991 Competing continuation Years 04-08;
177. April 20, 1988 NIH-IFN Award Letter 1986-87, 1987-88;
178. January 9, 1991 NIH/IFN Award Letter 1991-91;
179. Declaration for Patent Application Serial No. 07/791,898, filed November 13, 1991 signed by LeBowitz on 2/12/92;
180. May 6, 1992 IDS filed in U.S. Serial No. 07/791,898;
181. December 30, 1996 Office Action in U.S. Serial No. 08/464,364, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
182. October 15, 1997 Office Action in U.S. Serial No. 08/464,364, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
183. June 10, 1998 Amendment and Response in U.S. Serial No. 08/464,364, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
184. July 14, 1998 Office Action in U.S. Serial No. 08/464,364, Document 198, filed 02/03/2006, ADL 0000542-0000566,

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Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

185. January 14, 1999 Response and Amendment in U.S. Serial No. 08/464,364, ADL 0000570-0000588, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
186. March 11, 1999 Office Action in U.S. Serial No. 08/464,364 ADL 0000611-0000621, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
187. September 14, 1999 Declaration Under 37 C.F.R. §1.132 by David Baltimore including Exhibits A-J, ADL 0000625-0000696, Document 198-5, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
188. November 19, 1999 Office Action in U.S. Serial No. 08/484,364, ADL 0000708-0000716, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
189. May 30, 2000 Response and Amendment to November 29, 1999 Office Action in U.S. Serial No. 08/464,364, Document 214-2, filed 02/24/2006, in Civil Case 02 CV 11280 RWZ;
190. May 30, 2000 Response and Amendment in U.S. Serial No. 08/464,364, ADL 0000722-0000732, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
191. August 11, 2000 Office Action in U.S. Serial No. 08/464,364, ADL 0000822-0000833, Document 198-4, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
192. February 12, 2001 Response and Amendment in U.S. Serial No.

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08/464,364, ADL 0000843-0000853, Document 201, filed  
02/03/2006, in Civil Case 02 CV 11280 RWZ;

193. Declaration of David Baltimore Under Rule 1.132 & In re  
Brana dated February 2001, in U.S. Serial No. 08/464,364;

194. September 12, 2001 Response and Amendment in U.S. Serial  
No. 08/464,364, ADL 0000874-0000921, Document 201, filed  
02/03/2006, in Civil Case 02 CV 11280 RWZ;

195. September 12, 2001 Response and Amendment in U.S. Serial  
No. 08/464,364, ADL 0000874-0000888, Document 198, filed  
02/03/2006, in Civil Case 02 CV 11280 RWZ;

196. October 4, 2001 Examiner's Amendment in U.S. Serial No.  
08/464,364, ADL 0000924-0000953, Document 198-8, filed  
02/03/2006, in Civil Case 02 CV 11280 RWZ;

197. June 25, 2002 Complaint, 02 CV 11280 RWZ;

198. August 18, 2002 Declaration of Michael Karin (20 pgs),  
including Tabs 1-24, 02 CV 11280 RWZ;

199. August 19, 2002 Defendants Eli Lilly & Company Memorandum  
In Support Of Its Combined Motion To Dismiss Under  
Fed.R.Civ.P. 12(b)(6) and Motion for Summary Judgment of  
Invalidity Under 35 USC Section 102 and 112, including  
Exhibits A-D, 02 CV 11280 RWZ;

200. October 14, 2002 Declaration of Charles A. Dinarello, M.D.  
including Tabs A-D, 02 CV 11280 RWZ;

201. October 15, 2002 Declaration of Laurie H. Glimcher, M.D.

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including Tabs A-F, 02 CV 11280 RWZ;

202. October 16, 2002 Declaration of Brendan F. Boyce, M.B. Ch.B. including Tabs A-D, 02 CV 11280 RWZ;

203. October 16, 2002 Declaration of Dr. Thomas D. Gilmore including Exhibits A-C and D1-D24, 02 CV 11280 RWZ;

204. October 17, 2002 Plaintiffs Opposition to Defendants Eli Lilly & Com.'s Combined Motion to Dismiss Pursuant to Fed.R.Civ.P. 12(b)(6) and Motion for Summary Judgment Under 35 USC Sections 102 and 112 including Tabs A-M, 02 CV 11280 RWZ;

205. November 18, 2002 Defendant's Eli Lilly & Company Reply In Support of Its Combined Motion to Dismiss Under Fed.R.Civ.R.12(b)(6) And Motion For Summary Judgment of Invalidity Under 35 USC Sections 102 & 112, 02 CV 11280 RWZ;

206. November 21, 2002 Hearing for Summary Judgment, Computer-Aided Transcript, 02 CV 11280 RWZ;

207. May 12, 2003 Memo of Decision & Order, 02 CV 11280 RWZ;

208. May 27, 2003 Eli Lilly and Company's Answer To Plaintiffs Complaint And Counter Claims, 02 CV 11280 RWZ;

209. June 19, 2003 Plaintiffs' Answer to Defendants Eli Lilly & Company's Answer and Counterclaims, 02 CV 11280 RWZ with letter from Anne Marie Longobacco of Bromberg & Sunstein LLP;

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210. August 20, 2003 Plaintiffs Ariad Pharmaceutical, Inc. et al. Response to Eli Lilly and Company's First Set of Rule 33 Interrogatories (Nos. 1-4);
211. September 5, 2003 Eli Lilly & Company's Responses to Plaintiffs First Set of Interrogatories (Nos. 1-5);
212. October 6, 2003 Plaintiffs Ariad Pharmaceuticals, Inc. et al. Responses to Eli Lilly & Company's Second Set of Rule 33 Interrogatories (No. 5);
213. November 3, 2003 Tutorial Hearing, 02 CV 11280 RWZ;
214. November 3, 2003 Evidentiary Hearing before Honorable Rya W. Zobel, 02 CV 11280 RWZ;
215. November 24, 2003 Plaintiffs Opening Brief on Claim Construction, 02 CV 11280 RWZ;
216. November 24, 2003 Declaration of Laurie H. Glimcher, M.D.,;
217. November 24, 2003 Declaration of Vladimir V. Drozdoff in Support of Plaintiffs Opening Brief on Claim Construction, including Tabs 1-22, 02 CV 11280 RWZ;
218. November 24, 2003 Declaration of Dr. Thomas D. Gilmore, 02 CV 11280 RWZ;
219. November 24, 2003 Defendants Eli Lilly & Company Opening Claim Construction Brief (not signed), 02 CV 11280 RWZ, including Exhibits to Eli Lilly's Opening Claim Construction Brief, inc. Exhibits A-H and I & J, 02 CV 11280 RWZ;

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220. November 24, 2003 unsigned Defendant Eli Lilly and Company's Opening Claim Construction Brief, Document 198-3, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
221. December 22, 2003 Plaintiffs Opposition Brief on Claim Construction, 02 CV 11280 RWZ;
222. December 22, 2003 Declaration of Vladimir V. Drozdoff in Support of Plaintiffs Opposition Brief on Claim Construction, including Tabs 1-18, 02 CV 11280 RWZ;
223. December 22, 2003 Supplemental Declaration of Dr. Thomas D. Gilmore, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
224. December 22, 2003 Defendants Eli Lilly & Company's Opposition Claim Construction Brief, 02 CV 11280 RWZ;
225. January 9, 2004 Supplemental Declaration of Dr. Thomas D. Gilmore, 02 CV 11280 RWZ;
226. January 13, 2004 Markman Transcript Hearing before the Honorable Rya W. Zobel, U.S. District Judge, 02 CV 11280 RWZ;
227. January 13, 2004 Markman Hearing by Plaintiff, 02 CV 11280 RWZ;
228. January 13, 2004 Markman Hearing, A Scientific Tutorial by Eli Lilly & Comp. Paul H. Berghoff;
229. February 24, 2004 Motion For Leave To File Reply Memorandum

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In Support Of Defendant Eli Lilly And Company's Motion For Summary Judgment Of Invalidity Under 35 U.S.C. §102, Document 213-1, filed 02/24/2006, in Civil Case 02 CV 11280 RWZ;

230. March 3, 2004 Memorandum of Decision & Order re: Claim Construction, 02 CV 11280 RWZ;
231. March 3, 2004 Memorandum of Decision and Order, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
232. March 23, 2004 Subpoena in a Civil Case 02 CV 11280 RWZ Albert S. Baldwin, Jr., Ph.D.;
233. March 24, 2004 Plaintiffs Ariad Pharmaceuticals, Inc. et al. Supplemental Response to Eli Lilly & Company's First Set of Rule 33 Interrogatories (Nos. 1-5);
234. March 24, 2004 Eli Lilly & Company's Supplemental Response to Plaintiffs' First Set of Interrogatories (Nos. 1-5);
235. April 30, 2004 Plaintiffs Ariad Pharmaceuticals, Inc. et al. Second Supplemental Response to Eli Lilly & Company's First Set of Rule 33 Interrogatories (Nos. 1-5);
236. April 30, 2004 Eli Lilly & Company's Second Supplemental Responses to Plaintiffs' First Set of Interrogatories (Nos. 1-5);
237. May 7, 2004 Subpoena in a Civil Case 02 CV 11280 RWZ Chen-Ming Fan Ph.D.;
238. May 7, 2004 Subpoena in a Civil Case 02 CV 11280 RWZ David

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Baltimore, Ph.D.;

239. May 7, 2004 Subpoena in a Civil Case 02 CV 11280 RWZ  
Harinder Singh, Ph.D.;

240. May 7, 2004 Subpoena in a Civil Case 02 CV 11280 RWZ  
Jonathan H. LeBowitz, Ph.D.;

241. May 7, 2004 Subpoena in a Civil Case 02 CV 11280 RWZ  
Michael J. Lenardo M.D.;

242. May 12, 2004 Subpoena in a Civil Case 02 CV 11280 RWZ  
Ranjan Sen Ph.D.;

243. June 2, 2004 Plaintiffs Ariad Pharmaceuticals, Inc. et al.  
Responses to Eli Lilly & Company's Third Set of Rule 33  
Interrogatories (No. 6);

244. June 2, 2004 Plaintiffs Ariad Pharmaceuticals, Inc. et al.  
Third Supplemental Response to Eli Lilly & Company's First  
Set of Rule 33 Interrogatories (Nos. 1-5);

245. June 7, 2004 Hearing before Honorable Rya W. Zobel, without  
Jury;

246. June 28, 2004 Deposition of Jonathan H. Lebowitz in Civil  
Case 02 CV 11280 RWZ including deposition Exhibits 5-11 and  
13 attached with this Supplemental Information Disclosure  
Statement, namely: October 28, 1987 correspondence from  
Barbara Bakal Greene [LeBowitz 6/28/04 Exh 5]; May 19, 1987  
Notice of Grant Award [LeBowitz 6/28/04 Exh 6]; July 26,  
1988 Notice of Grant Award [LeBowitz 6/28/04 Exh 7];  
December 19, 1989 Notice of Grant Award [LeBowitz 6/28/04

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Exh 8]; April 23, 1990 Notice of Grant Award [LeBowitz 6/28/04 Exh 9]; Set of hand written notes [LeBowitz 6/28/04 Exh 10]; Set of hand written notes [LeBowitz 6/28/04 Exh 11]; and Set of hand written notes [LeBowitz 6/28/04 Exh 13] (deposition Exhibits 2 and 14 are copies of the subject patent, deposition Exhibit 12 is plaintiffs' privileged log, and deposition Exhibits 1, 3 and 4 have been submitted as items 164, 2 and 167, respectively, in Patentees' August 8, 2005 Information Disclosure Statement);

247. June 30, 2004 Deposition of Harinder Singh, Ph.D. in Civil Case 02 CV 11280 RWZ including deposition Exhibits 21-25 attached with this Supplemental Information Disclosure Statement, namely: February 25, 2988 American Type Culture Collection [Singh 6/30/04 Exh 21]; Set of hand written notes [Singh 6/30/04 Exh 22]; Set of hand written notes [Singh 6/30/04 Exh 23]; Set of hand written notes [Singh 6/30/04 Exh 24] and Set of hand written notes [Singh 6/30/04 Exh 25] (deposition Exhibits 17, 18, 27, 28, 30 and 31 have been submitted as items 163, 1, 26, 27, 76 and 100, respectively in Patentees' August 8, 2005 Information Disclosure Statement);
248. August 23, 2004 Defendant's Exhibit 45 - Asserted Claims Against EVISTA;
249. August 23, 2004 Deposition of Dr. David Baltimore in Civil Case 02 CV 11280 RWZ;
250. August 23, 2004 Videotaped Deposition of Dr. David Baltimore, pgs. 1-4, and 85-87 in Civil Case 02 CV 11280 RWZ;

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251. September 30, 2004 Deposition of Dr. Phillip A. Sharp in Civil Case 02 CV 11280 RWZ including deposition Exhibits 87-89 attached with is Supplemental Information Disclosure Statement, namely: February 13, 1986 correspondence from Brian W. Kimes, Ph.D. [Sharp 9/30/04 Exh 87]; April 30, 1986 Notice of Grant Award [Sharp 9/30/04 Exh 88]; and November 3, 1986 Notice of Grant Award [Sharp 9/30/04 Exh 89] (deposition Exhibits 85 and 86 have been submitted as items 29 and 28 in Patentees' August 8, 2005 Information Disclosure Statement);
252. October 12, 2004 Deposition of Ranjan Sen in Civil Case 02 CV 11280 RWZ;
253. October 18, 2004 Eli Lilly & Company's Response to Plaintiffs' Second Set of Requests for Admission to Eli Lilly & Company (Nos. 19-23);
254. October 21, 2004 Deposition of Chen-Ming Fan in Civil Case 02 CV 11280 RWZ;
255. October 22, 2004 Deposition of Michael J. Lenardo, M.D. in Civil Case 02 CV 11280 RWZ;
256. October 26, 2004 Deposition of Albert S. Baldwin, Jr. Ph.D. in Civil Case 02 CV 11280 RWZ;
257. November 2, 2004 Eli Lilly & Company's Third Supplemental Responses to Plaintiffs First Set of Interrogatories (Nos. 1-5);
258. November 10, 2004 Deposition of Thomas P. Maniatis, Ph.D. in Civil Case 02 CV 11280 RWZ;

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259. November 12, 2004 Plaintiffs Ariad Pharmaceuticals, Inc. et al. Responses to Eli Lilly & company's Fourth Set of Rule 33 Interrogatories (Nos. 7-8);
260. December 1, 2004 Deposition of Dr. Patrick Baeuerle in Civil Case 02 CV 11280 RWZ;
261. December 13, 2004 Defendant's Response to Plaintiffs Fourth Set of Interrogatories (Nos. 8-18);
262. December 15, 2004 Plaintiffs Ariad Pharm., Inc. et al. Responses to Eli Lilly & Com.'s First Set of Requests For Admission (Nos. 1-25), 02 CV 11280 RWZ;
263. December 15, 2004 Eli Lilly & Company's Responses to Plaintiffs' Third Set of Requests for Admission (Nos. 24-45);
264. December 15, 2004 Plaintiffs Ariad Pharmaceuticals, Inc. et al. Responses to Eli Lilly & Company's Fifth Set of Rule 33 Interrogatories;
265. March 14, 2005 Plaintiffs' Supplemental Response to Eli Lilly's Fourth Set of Rule 33 Interrogatories (Nos. 7-8);
266. March 14, 2005 Eli Lilly & Company's Response to Plaintiffs Fifth Set of Interrogatories;
267. June 6, 2005 Order Concerning Discovery & Stay of Proceedings, 02 CV 11280 RWZ;
268. September 7, 2005 Expert Report of Peter Barnes, Ph.D. in

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Civil Case 02 CV 11280 RWZ;

269. September 9, 2005 Expert Report of Dr. Laurie H. Glimcher in Civil Case 02 CV 11280 RWZ;
270. September 9, 2005 Expert Report of Dr. Laurie H. Glimcher, pages cover, 9, 14-15, and 32 in Civil Case 02 CV 11280 RWZ;
271. September 9, 2005 Expert Report of David Latchman, DSc., Ph.D., pgs. Cover, 5 and 11, in Civil Case 02 CV 11280 RWZ;
272. September 15, 2005 Plaintiffs' Third Supplemental Response to Eli Lilly & Company's First Set of Interrogatories (Nos. 1-4);
273. Expert Report of David Latchmann, Dsc., Ph.D., dated September 5, 2005, including copies of the following referenced in the report: Altavilla, Cardiovascular Research (2001) 52:143-152; January 13, 2004 Markman Hearing; November 2, 2003 Tutorial Hearing; Baldwin, Jr., Annu. Rev. Immunol. (1996) 14:649-81; Baltimore, Nature (1988) 335:395-396; Bielinska, Science (1990) 250:997-1000; Blackwell, Arthritis & Rheumatism (2004) 50:2675-2684; Blanco-Colio, Circulation (2000) 102:1020-1026; Böhnlein, Cell (1988) 53:827-836; Budhram-Mahadeo, The Journal of Biological Chemistry (1996) 271:9108-9113; Cavazzana-Calvo, Nature (2004) 427:779-781; Cross, Science (1989) 244:466-469; Dang, Clinical Cancer Research (1999) 5:471-474; Davis, Science (1991) 253:1268-1271; Fan, The EMBO Journal (1989) 8:101-110; Fawell, Proc. Natl. Acad. Sci. USA (1994) 91:664-668; Friedman, Nature (1988) 335:452-454; Goodbourn, Proc. Natl. Acad. Sci. USA (1988) 85:1447-1451; Hoag,

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Nature (2005) 435:530-531; Hölschermann, Circulation (1997) 96:4232-4238; Kabouridis, The Journal of Immunology (2002) 169:2587-2593; Cirriculum Vitae Professor David S. Latchman; Lenardo, Proc. Natl. Acad. Sci. USA (1988) 85:8825-8829; Leung, Nature (1988) 333:776-778; Ariad et al. v. Eli Lilly and Company A Scientific Tutorial; Ariad et al. v. Eli Lilly and Company Markman Presentation; Mann, The Journal of Clinical Investigation (2000) 106:1071-1075; Morishita, Proc. Natl. Acad. Sci. USA (1995) 92:5855-5859; Morishita, Nature Medicine (1997) 3:894-899; Morris, Molecular and Cellular Biology (1994) 14:6907-6914; March 3, 2004 Memorandum of Decision and Order; Ruben, Science (1988) 241:89-92; Sawa, Circulation (1997) 96[supp II]:II280-II285; Scott, Genes & Development (1993) 7:1266-1276; Selected pages of NF- $\kappa$ B Tutorial; Ting, Science (2002) 298:1189-1190; Tomita, Arthritis & Rheumatism (1999) 42:2532-2542; Verma, Nature (1997) 389:239-242 and Latchman, Eukaryotic Transcription Factors, (2004) Fourth Edition Book;

274. Expert Report of Dr. Jesus Egido, dated September 9, 2005, including: Report of the Dietary Guidelines <<http://www.nal.usda.gov/fnic/Dietary/director.htm>>; Baldwin Jr., The Journal of Clinical Investigation (2001) 107:3-6; Bellido, Am. J. Clin. Nutr. (2004) 80:1487-91; The Holy Bible <<http://etext.lib.virginia.edu/kjv/browse.html>>; Blanco-Colio, Circulation (2000) 102:1020-1026; Burns, J. Agric. Food Chem. (2002) 50:4096-4102; Dell'Agli, Cardiovascular Research (2004) 63:593-602; Deo, Journal of the American College of Cardiology (2004) 44:1812-8; Abbreviated CV of Jesus Egido MD; Manuscript; Gaziano, The New England Journal of Medicine (1993) 329:1829-34; Ghanim, Circulation (2004) 110:1564-1571; Hofmann, Diabetologia

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(1999) 42:222-232; Holmes-McNary, Cancer Research (2000) 60:3477-3483; López-Vélez, Critical Reviews in Food Science and Nutrition (2003) 43:233-244; Manna, The Journal of Immunology (2000) 164:6509-6519; Martin-Ventura, Stroke (2004) 35:458-463; March 3, 2004 Memorandum of Decision And Order; Richie, Circulation (1998) 98:1707-1713; Leger, Then Lancet (1979) 1:1017-1020 and Tsang, British Journal of Nutrition (2005) 94:170-181;

275. Expert Report of Peter Barnes, Ph.D., dated September 9, 2005 including: Appendix B Baltimore Deposition; Appendix C Baldwin Deposition; January 13, 2004 Markman Hearing; November 3, 2003 Tutorial Hearing; Baeuerle, Cell (1996) 87:13-20; Baldwin, Jr. Annu. Rev. Immunol. (1996) 14:649-81; Barnes, D.M., D.Sc., The New England Journal of Medicine 1997 336:1066-1071; Beg, Nature, (1995) 376:167-170; Blackwell, Am. J. Respir. Cell Mol. Biol. (1997) 17:3-9; Brown, Proc. Natl. Acad. Sci. USA (1993) 90:2532-2536; Collins, The Journal of Clinical Investigation (2001) 107:255-264; Resume of Peter John Barnes; Han, The Journal of Biological Chemistry (1999) 274:939-947; Hoffman, Science (2002) 298:1241-1245; Ito, Nucleic Acids Research (1994) 22:3787-3792; Klement, Molecular and Cellular Biology (1996) 16:2341-2349; Li, J. Exp. Med. (1999) 11:1839-1845; Ariad et al. v. Eli Lilly and Company A Scientific Tutorial; Ariad et al. v. Eli Lilly and Company Markman Presentation; Noble, J. Exp. Med. (1996) 183:2373-2378; March 3, 2004 Memorandum of Decision and Order; Scott, Genes & Development (1993) 7:1266-1276; Selected pages of NF- $\kappa$ B Tutorial; and Sun, Science (1993) 259:1912-1915;

276. Expert Report of Stavros C. Manolagas, M.D., Ph.D., dated

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September 9, 2005 including: Physicians' Desk Reference (1970) 24<sup>th</sup> Edition; Physicians' Desk Reference (1985) 39<sup>th</sup> Edition; Adams, Journal of Bacteriology (2003) 185:1174-1180; Aljada, The Journal of Clinical Endocrinology & Metabolism (1996) 84:3386-3389; Curriculum Vitae of Stavros C. Manolagas, M.D., Ph.D. last updated 8/1/05; Declaration of Stavros Manolagas, M.D., Ph.D.; January 13, 2004 Markman Hearing; November 2, 2003 Tutorial Hearing; Auphan, Science (1995) 270:286-290; Baeuerle, Advances in Immunology (1997) 65:111-137; Baldwin, Jr., Annu. Rev. Immunol. (1996) 14:649-81; Baldwin, Jr., The Journal of Clinical Investigation (2001) 107:3-6; Declaration of David Baltimore under Rule 1.132 and In re Brana (February 2001); Bantel, The American Journal of Gastroenterology (2000) 95:3452-3457; Belido, The Journal of Clinical Investigation, Inc. (1995) 95:2886-2895; Annual Meeting...Atlantic City June 16-20, 1963, the Journal of the American Medical Association 183:166-169; Brini, Eur. Cytokine Net, (1990) 1:131-139; Caulin-Glaser, J. Clin. Invest (1996) 98:36-42; Chadwick, PNAS (2005) 102:2543-2548; Chen, The Journal of Biological Chemistry (2005) 280:4632-4638; Deshpande, AJRI (1997) 38:46-54; Hughes, British Medical Journal (1983) 287:23-24; Emmel, Science (1989) 246:1617-1620; Evans, Endocrinology (2002) 143:3785-3795; Forsblad, Arthritis Research & Therapy (2003) 5:R202-R209; Franta, The EMBO Journal (1994) 13:861-870; Gao, PNAS (2004) 101:16618-16623; Ghisletti, Molecular and Cellular Biology (2005) 25:2957-2968; Hahn, (1950) pgs. 274-281; Harnish, Endocrinology (2000) 141:3403-3411; Hench, Nobel Lecture (1950) 311-341; Hölschermann, Circulation (1997) 96:4232-4238; Ide, J. Nutr. (2001) 131:1020S-1026S; Jilka, Science (1992) 257:88-91; Kopp, Science (1994) 265:956-959; Kousteni, Cell (2001) 104:719-730; Kousteni, Science (2002)

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 60 of 103 of September 28, 2006 Amendment

298:843-846; Kousteni, The Journal of Clinical Investigation (2003) 111:1651-1664; Krönke, Proc. Natl. Acad. Sci. USA (1984) 81:5214-5218; Kurebayashi, J. Steroid Biochem. Molec. Biol. (1997) 60:11-17; Lean, The Journal of Clinical Investigation (2003) 112:915-923; Lefering, Critical Care Medicine (1995) 23:1294-1303; Ariad et al. v. Eli Lilly and Company A Scientific Tutorial; Ariad et al. v. Eli Lilly and Company Markman Presentation; Lin, The Journal of Clinical Investigation (1997) 100:1980-1990; Luborsky, Human Reproduction (2002) 18:199-206; Manolagas, Calcified Tissue International (1992) 50:199-202; Manolagas, Osteoporosis Int. (1993) Suppl. 1:S114-S116; Manolagas, Therapeutic Research (1994) 15:27-33; Manolagas, Current Opinion in Endocrinology and Diabetes (1994) 275-281; Manolagas, Int. J. Immunopharmac (1995) 17:109-116; Manolagas, The New England Journal of Medicine (1995) 332:305-311; Manolagas, Endocrine Reviews (2000) 21:115-137; Manolagas, The Endocrine Society (2002) 57:385-409; Manolagas, Kidney International (2004) 66:S41-S49; Manson, Biochemical Society Transactions (2000) 28:7-12; McCaffrey, Nucleic Acids Research (1994) 22:2134-2142; Metka, Fertility and Sterility (1992) 57:37-41; Nelson, JAMA (2002) 288:872-881; March 3, 2004 Memorandum Of Decision and Order; June 8, 2005 Order Granting/Denying Request For Ex Parte Reexamination issued by the PTO; Pan, Biochemical Pharmacology (2000) 59:357-367; A Modern Herbal Garlic <<http://www.botanical.com/botanical/mgmh/g/garlic06.html>>; Plotkin, The Journal of Biological Chemistry (2005) 280:7317-7325; Pottratz, The Journal of Clinical Investigation, Inc. (1994) 93:944-950; Ray, The Journal of Biological Chemistry (1994) 269:12940-12946; Ray, FEBS Letters (1997) 409:79-85; April 4, 2005 Request For Reexamination Pursuant To 35 U.S.C. §302; Scheinman,

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 61 of 103 of September 28, 2006 Amendment

Science (1995) 270:283-286; Scheinman, Molecular and Cellular Biology (1995) 15:943-953; Schmidt, Journal of Virology (1990) 64:4037-4041; Selected pages of NF- $\kappa$ B Tutorial; Simoncini, Circ. Res. (2000) 87:19-25; Singh, The Journal of Biological Chemistry (1995) 270:24995-25000; Speir, Circ. Res. (2000) 87:1006-1011; Stein, Molecular and Cellular Biology (1995) 15:4971-4979; Sun, Biochemical and Biophysical Research Communications (1998) 244:691-695; Synthetic Generic Conjugated Estrogens: Timeline <<http://www.fda.gov/cder/news/cetimeline.htm>>; Mukherjee, The Journal of Biological Chemistry (2003) 278:11746-11752; The Originals of Tea <<http://www.tea.co.uk/tGloriousT/index.htm>>; Monograph <<http://www.nutrisana.com/html/Monograph-Curcuma.html>>; Tyree, Journal of Steroid Biochemistry & Molecular Biology (2002) 80:291-297; Weissmann, Scientific American (1991) pgs. 84-90; Yan, The Journal of Biological Chemistry (1999) 274:36631-36636; Yang, J. Nutr. (1998) 128:2334-2340; Yin, Nature (1998) 396:77-80; Yuan, Science (2001) 293:1673-1677 and Zang, Journal of Neuroimmunology (2002) 124:106-114;

277. October 3, 2005 Eli Lilly and Company's Fifth Supplemental Responses To Plaintiff's First Set of Interrogatories (Nos. 1-5), pgs. 1-6, in Civil Case 02 CV 11280 RWZ;
278. October 20, 2005 Expert Report of Jeffrey V. Ravetch, M.D., Ph.D., pgs. 1-43 with Certificate of Service, in Civil Case 02 CV 11280 RWZ;
279. October 20, 2005 Expert Report of Jeffrey V. Ravetch, M.D., Ph.D., pgs. Cover, 14-15, and 36, Document 198-10, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

Applicants: David Baltimore et al.  
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280. October 21, 2005 Expert Report of Dr. Stephen Prescott, pgs. Cover, 52-53 and 60, Document 198-11, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

281. October 21, 2005 Rule 26(A)(2) Rebuttal Report of Thomas R. Kadesch, Ph.D., Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

282. October 21, 2005 Rule 26(a)(2) Rebuttal Report of George R. Stark, Ph.D., Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

283. Expert Report of Dr. Gordon Bernard, dated October 21, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-125 attached with this Fourth Supplemental Information Disclosure Statement, namely: Physicians' Desk Reference, 24<sup>th</sup> Ed. (1970) various pages of the Generic and Chemical Name Index; U.S. Patent No. 4,775,624, issued October 4, 1988, Bang et al.; U.S. Patent No. 6,410,516 B1, issued June 25, 2002, Baltimore et al.; Abraham et al., JAMA (1995) 273:934-941; Abraham et al., The Lancet (1998) 351:929-933; Abraham et al., Am. J. Physiol. Lung Cell Mol. Physiol (2000) 279:L1137-L1145; Abraham E., Crit. Care Med. (2003) 31[Suppl.]:S195-S199; Alberti, et al., Intensive Care Med (2002) 28:108-121; Aljada et al., The Journal of Clinical Endocrinology & Metabolism (1996) 84:3386-3389; Angus et al., Crit Care Med (2001) 29:1303-1310; Angus et al., Crit Care Med (2004) 32:2199-2206; Angus et al., Crit Care Med (2001) 29:1303-1310; Djillali et al. JAMA (2005) 288:862-871; Baldwin Jr., A.S., Annu. Rev. Immunol. (1996) 14:649-681; Baumgartner et al. The Lancet (1985) pp. 59-63; Bernard et al., N. Engl. J. Med. (2001) 344:699-709; Curriculum Vitae of Gordon R. Bernard, M.D. updated

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 63 of 103 of September 28, 2006 Amendment

08/24/05; Bone et al., *N. Engl. J. Med.* (1987) 317:653-658;  
Bone et al., *Critical Care Medicine* (1995) 23:994-1006;  
Branson et al., *The Lancet* (1983) pp. 1165-1168; Brun-  
Buisson et al., *JAMA* (1995) 274:968-974; Brueckmann M.,  
Thromb Haemost (2003) 90:1123-1126; Brueckmann et al.,  
Inflamm. Res. (2004) 53:528-533; Brueckmann et al., Thromb  
Haemost (2003) 89:149-160; Brun-Buisson C., *Intensive Care  
Med* (2004) 30:580-588; Bryniarski et al., *Inflammation*  
(2003) 27:333-340; Bunnell et al., *Crit. Care Med.* (2000)  
28:2713-2720; Cohen and Carlet, *Crit. Care Med.* (1996)  
24:1431-1440; Cohen J., *Nature* (2002) 420:885-891; Collart  
et al., *Molecular and Cellular Biology* (1990) 10:1498-1506;  
Colucci et al., *J. Clin. Invest.* (1984) 74:200-204; Comp  
and Esmon, *J. Clin. Invest.* (1981) 68:1221-1228; Cooper and  
Stewart, *N. Engl. J. Med.* (2003) 348:727-734; Cronin et  
al., *Crit. Care Med.* (1995) 23:1430-1439; de Kleijn et al.,  
*Crit. Care Med.* (2003) 31:1839-1847; de Hooge et al.,  
*Osteo. Arthritis and Cartilage* (2005) 13:66-73; de Pont et  
al., *Critical Care* (2005) 9:R490-R497; Derhaschnig et al.,  
*Blood* (2003) 102:2093-2098; Derkx, et al., *Clinical  
Infectious Diseases* (1999) 28:770-777; Bernard et al., *N.  
Engl. J. Med.* (2001) 344:699-709; Bernard G.R., *Intensive  
Care Med.* (2003) 29:894-903; Dhainaut et al., *Thromb  
Haemost* (2003) 90:642-653; Emerick et al., *The Pharmacology  
and Toxicology of Proteins* (1987) pp. 351-367; Esmon et  
al., *The Journal of Biological Chemistry* (1976) 251:3052-  
3056; Esmon C.T., *J. Thromb. Haemost* (2005) 3:1910-1911;  
FDA Clinical Review BLA#125029/0 pp. 78-161; Feistritzer  
and Riewald, *Blood* (2005) 105:3178-3184; Finfer et al.,  
*Intensive Care Med.* (2004) 30:589-596; Fisher et al., *N.  
Engl. J. Med.* (1996) 334:1697-1702; Flournoy et al., *Med.  
Microbiol. Immunol.* (1986) 175:221-227; Giroir et al.,  
*Lancet* (1997) 350:1439-1443; Glick and Opal, *Drugs* (2004)

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 64 of 103 of September 28, 2006 Amendment

64:837-859; Granowitz et al., Blood (1993) 82:2985-2990; Greenman et al., JAMA (1991) 266:1097-1102; Griffin et al., J. Clin. Invest. (1981) 68:1370-1373; Gruber and Griffin, Blood (1992) 79:2340-2348; Gruber et al., Lancet (1993) 342:1275-1276; Hahn et al., from the Streptococcal Disease Laboratory (1950) pp. 274-281; Hinshaw et al., Circulatory Shock (1985) 16:265-277; Hinshaw et al, Surgery Gynecology & Obstetrics (1986) 163:335-344; Hiscott et al., Molecular and Cellular Biology (1993) 13:6231-6240; Hooper et al., The Journal of Immunology (1998) 161:2567-2573; Hotchkiss and Karl The New England Journal of Medicine (2003) 348:138-150; Beckman et al., Intellectual Property Owners A s s o c i a t i o n  
<[http://www.ipo.org/Template.cfm?Section=National\\_Inventor\\_Of\\_The\\_Year\\_Award1&...](http://www.ipo.org/Template.cfm?Section=National_Inventor_Of_The_Year_Award1&...)>; Joyce and Grinnell, Crit. Care Med. (2002) 30[Suppl]:S288-S293; Joyce et al.,, The Journal of Biological Chemistry (2001) 276:11199-11203; Kalil et al., Shock (2004) 21:222-229; Keh et al., Am. J. Respir. Crit. Care med. (2003) 167:512-520; Kisiel et al., Biochemistry (1976) 15:4893-4900; Klein et al., J. Clin. Invest. (2005) 115:860-869; Kremer et al, Acta Maematol (1996) 95:268-273; Lefering and Neugebauer, Critical Care Medicine (1995) 23:1294-1303; Levin et al., "Lancet (2000) 356:961-967; Macias et al., clin. Pharmacol. Ther. (2002) 72:391-402; Mammen et al., Thrombosis et Diathesis Haemorrhagica (1961) 5:1-17; Marsik et al., Clinical Immunology (2005) 114:293-298; Martin et al., N. Engl. J. Med (2003) 348:1546-1554; McCloskey et al., Ann. Intern. Med. (1994) 121:1-5; Mifflin et al., Molecular Pharmacology (2004) 65:470-478; Mori and Prager, Blood (1996) 87:3410-3417; Nick et al., Blood (2004) 104:3878-3885; Novoa et al., Preparative Biochemistry (1976) 6:307-329; Opal et al., Crit. Care Med. (1997) 25:1115-1124; Owen and Esmon,

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 65 of 103 of September 28, 2006 Amendment

The Journal of Biological Chemistry (1981) 256:5532-5535; Padkin et al., Crit. Care Med. (2003) 31:2332-2338; Panacek et al., crit. Care Med. (2004) 32:2173-2182; Parrillo et al., Annals of Internal Medicine (1990) 113:227-242; Parrillo J.E., The New England Journal of Medicine (1993) 328:1471-1477; Patil et al., Immunol. Invest. (2004) 33:213-233; Pedersen et al., Pflugers Arch - Eur. J. Physiol (2003) 446:9-16; Phase 1 Clinical Studies <<file:///S:/William A\Lindsay References\Phase 1 Clinical Studies.htm>>; Phase 2 Clinical Studies <<file:///S:/William A\Lindsay References\Phase 2 Clinical Studies.htm>>; Phase 3 Clinical Studies <<file:///S:/William A\Lindsay References\Phase 3 Clinical Studies.htm>>; Preas II et al., Blood (1996) 88:2465-2472; Quesado et al., JAMA (1993) 269:2221-2227; Rangel-Frausto et al., JAMA (1995) 273:117-123; Sakata et al., Proc. Natl. Acad. Sci. USA (1985) 82:1121-1125; Scheinman et al., Molecular and Cellular Biology (1995) 15:943-953; Scheinman et al., Science (1995) 270:283-286; Schlaak et al., Scand. J. Immunol. (2001) 54:396-403; Seegers et al., Thrombosis Research (1976) 8:543-552; Soop et al., Shock (2003) 19:503-507; Sprung et al., N. Engl. J. Med. (1984) 311:1137-1143; Stein and Yang, Molecular and Cellular Biology (1995) 15:4971-4979; Stenflo J., the Journal of Biological Chemistry (1976) 251:355-363; Suffredini et al, The Journal of Immunology (1995) 155:5038-5045; Satoshi et al, Eur. J. Immunol. (2005) 35:460-468; Taylor et al., J. Clin. Invest. (1987) 79:918-925; U.S. Patent No. 5,009,889, issued April 23, 1991, Taylor Jr., et al.; Van Amersfoort et al., Clincial Microbiology Reviews (2003) 16:379-414; von der Möhlen et al., the Journal of Infectious Diseases (1995) 172:144-151; van der Poll et al., J. Clin. Invest. (1996) 97:713-719; van der Poll et al., J. Clin. Endocrinol. Metab. (1996)

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 66 of 103 of September 28, 2006 Amendment

81:3604-3606; van der Poll et al., Blood (1997) 89:3727-3734; van Hinsbergh et al., Blood (1985) 65:444-451; Van Zee et al., The Journal of Immunology (1995) 154:1499-1507; Verbon et al., The Journal of Immunology (2001) 166:3599-3605; Hinshaw et al., N. Engl. J. Med. (1987) 317:659-665; Wheeler and Bernard, N. Engl. J. Med. Current Concepts (2005) 340:207-214; Wong et al., Arthritis & Rheumatism (2003) 48:1177-1189; Wuestefeld et al., The Journal of Biological Chemistry (2003) 278:11281-11288; Eli Lilly and Company Briefing Document for XIGRIS™ for the Treatment of Severe Spesis (2001) pp. 2-189; XIGRIS™ Drotrecogin alfa (activated) pp. 1-9; Macias et al., Critical Care (2005) 9[Suppl.]:S38-S45; Zeng et al., Crit. Care Med. (2004) 32 [Suppl]:S302-S308; Crit. Care Med. (1997) 25:1095-1100; Ziegler et al., N. Engl. J. Med. (1982) 307:1225-1230; Ziegler et al., N. Engl. J. Med. (1991) 324:429-436;

284. Expert Report of Stavros C. Manolagas, M.D., Ph.D., dated October 21, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-115 attached with this Fourth Supplemental Information Disclosure Statement, namely: Adams et al., Journal of Bacteriology (2003) 185:1174-1180; Aljada et al., The Journal of Clinical Endocrinology & Metabolism (1996) 84:3386-3389; Curriculum Vitae of Stavros C. Manolagas, J.D., Ph.D. updated 8/1/05; Aronica and Katzenellenbogen, Molecular Endocrinology (1993) 7:743-752; Azria and Avioli, Principles of Bone Biology (1996) Chapter 78 pp. 1083-1097; Baldwin Jr. A. S., Annu. Rev. Immunol. (1996) 14:649-681; Baldwin Jr. A. S., The Journal of Clinical Investigation (2001) 107:3-6; Benten et al., Endocrinology (2001) 142:1669-1677; Berg et al., The Journal of Biological Chemistry (1995) 270:15447-15450; Biskobing D.M., Chest (2002) 121:609-620; Black et al., J.

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 67 of 103 of September 28, 2006 Amendment

Clin. Invest. (1994) 93:63-69; Blum et al., The American Jurnal of Cardiology (2000) 86:892-895; Bond et al., FEBS Letters (1998) 435:29-34; Bunone et al., The EMBO Journal (1996) 15:2174-2183; Chadwick et al., PNAS (2005) 102:2543-2548; Chaisson et al., the Journal of Biological Chemistry (2004) 279:54841-54848; Chen et al., The Journal of Biological Chemistry (2005) 280:4632-4638; Cho and Katzenellenbogen, Molecular Endocrinology (1993) 7:441-452; Coleman and Smith, Frontiers in Bioscience (2001) 6:1379-1391; Coleman et al., The Journal of Biological Chemistry (2003) 278:12834-12845; Coleman et al., Biochemical and Biophysical Research Communication (2004) 323:332-338; Compston J.E., Physiological Reviews (2001) 81:419-447; Cummings et al., JAMA (1999) 281:2189-2197; Delmas et al., N. Engl. J. Med. (1997) 337:1641-1647; Deshpande et al., AJRI (1997) 38:46-54; Doran et al., Journal of Bone and Mineral Research (2001) 16:2118-2125; Draper et al., Journal of Bone and Mineral Research (1996) 11:835-842; Duan et al., Endocrinology (1998) 139:1981-1990; El-Tanani and Green, Molecular Endocrinology (1997) 11:928-937; Eriksen et al., Journal of Bone and Mineral Research (1999) 14:1217-1221; Erlandsson et al., Journal of Endocrinology (2002) 175:319-327; Synthetic Generic Conjugated Estrogens: Time line ( 2 0 0 3 )  
<<http://www.fda.gov/cder/news/cetimeline.htm>>; Evans et al., Endocrinology (1994) 134:2283-2288; Franzoso et al., Genes & Development (1997) 11:3482-3496; Farsetti et al., Endocrinology (1998) 139:4581-4589; Fleisch H., Bisphosphonates in Bone Disease (1997) 3<sup>rd</sup> Ed. Pp. 5-67; Fleisch H., Bisphosphonates in Bone Disease (1997) 3<sup>rd</sup> Ed. Pp. 5-163; Frolik et al., Bone (1996) 18:621-627; Ghisletti et al., Molecular and Cellular Biology (2005) 25:2957-2968; Harnish et al., Endocrinology (2000) 141:3403-3411;

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 68 of 103 of September 28, 2006 Amendment

Horowitz et al., J. Clin. Invest. (1989) 83:149-157; Hughes et al., Nature Medicine (1996) 2:1132-1136; Jilka et al., Science (1992) 257:88-91; Jimi et al. Nature Medicine (2004) 10:617-624; Proceedings of ASCO Volume 17 (1998) p.122a; Kousteni et al., Cell (2001) 104:719-730; Kousteni et al., Science (2002) 298:843-846; Kousteni et al., J. Clin. Invest. (2003) 111:1651-1664; Krämer et al., The Journal of Biological Chemistry (1995) 270:6577-6583; Le Mellay et al., The Journal of Biological Chemistry (1997) 272:11902-11907; Levin E.R., TEM (1999) 10:374-377; Liu et al., The Journal of Immunology (2000) 164:4277-4285; Liu et al., Journal of the National Cancer Institute (2003) 95:1586-1597; Lubrosky et al., Human Reproduction (2002) 18:199-206; Manolagas S. C., Endocrine Reviews (2000) 21:115-137; Manolagas and Kousteni, Endocrinology (2001) 142:2200-2204; Manolagas et al., Abstract The Endocrine Society (2002) pp. 385-409; Manolagas et al., Kidney International (2004) 66:S41-S49; Marino et al., Molecular and Cellular Endocrinology (2001) 182:19-26; Martino et al., J. Natl. Cancer Inst. (2004) 96:1751-1761; McDonnell D.P., TEM (1999) 10:301-311; McDonnell D.P., Endocrinology (2003) 144:4237-4240; Metka et al., Fertility and Sterility (1992) 57:37-41; Mundy et al., Osteoporosis (1996) pp. 301-313; Physician's Guide to Prevention And Treatment of Osteoporosis (2003); Nelson et al., JAMA (2002) 288:872-881; Norfleet et al., FASEB J. (2000) 14:157-165; O'Brien et al., Am. J. Physiol. Endocrinol. Metab (2005) 289:E784-E793; Papapoulos S.E., Osteoporosis (1996) Chapter 64 1209-1234; Parfitt A.M., Journal of Cellular Biochemistry (1994) 55:273-286; Parfitt et al., Journal of Bone and Mineral Research (1996) 11:150-159; U.S. Patent No. 5,393,763, issued February 28, 1995, Black et al.; U.S. Patent No. 5,439,923, issued August 8, 1995,

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 69 of 103 of September 28, 2006 Amendment

Cullinan; U.S. Patent No. 5,439,931, issued August 8, 1995  
Sales; U.S. Patent No. 5,441,966, issued August 15, 1995,  
Dodge; U.S. Patent No. 5,446,053, issued August 29, 1995,  
Keohane; U.S. Patent No. 5,451,589, issued September 19,  
1995, Dodge; U.S. Patent No. 5,451,590, issued September  
19, 1995, Dodge; U.S. Patent No. 5,457,117, issued October  
10, 1995, Black et al.,; U.S. Patent No. 5,461,064, issued  
October 24, 1995, Cullinan; U.S. Patent No. 5,462,949,  
issued October 31, 1995, Jones et al.,; U.S. Patent No.  
5,534,526, issued July 9, 1996, Cullinan; U.S. Patent No.  
5,574,048, issued November 12, 1996, Cullinan; U.S. Patent  
No. 5,593,987, issued January 14, 1997, Cullinan et al.;  
U.S. Patent No. 5,596,004, issued January 21, 1997, Dodge;  
U.S. Patent No. 6,417,198, issued July 9, 2002, Bryant et  
al.; Penolazzi et al., International Journal of Molecular  
Medicine (2004) 14:145-152; Pfahl M., Endocrine Reviews  
(1993) 14:651-658; Poli et al., EMBO Journal (1994)  
13:1189-1196; Power et al., Science (1991) 254:1636-1639;  
Razandi et al., Molecular Endocrinology (1999) 13:307-319;  
Reed et al., Anti-Cancer Drugs (2005) 16:559-567; JAMA  
(2002) 288:321-333; Rodan and Fleisch, J. Clin. Invest.  
(1996) 97:2692-2696; Scheinman et al., Science (1995)  
270:283-286; Scheinman et al., Molecular and Cellular  
Biology (1995) 15:943-953; Schindler and Baichwal,  
Molecular and Cellular Biology (1994) 14:5820-5831; Sims et  
al., J. Clin. Invest. (2004) 113:379-389; Sims et al.,  
Journal of Bone and Mineral Research (2005) 20:1093-1102;  
Smith et al., Molecular Endocrinology (1997) 11:657-666;  
Stein and Yang, Molecular and Cellular Biology (1995)  
15:4971-4979; Tam et al., Science (1986) 234:1234-1237;  
Tang et al., PNAS (2005) 102:5132-5137; Teitelbaum S.L.,  
Science (2000) 289:1504-1508; Tesarik and Mendoza, J. Clin.  
Endocrinol. Metab. (1995) 80:1438-1443; Treilleux et al.,

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
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Molecular Endocrinology (1997) 11:1319-1331; Truss and Beato, Endocrine Reviews (1993) 14:459-479; U.S. Patent No. 6,545,027, issued April 8, 2003, Berg et al.; van de Stople et al., The Journal of Biological Chemistry (1994) 269:6185-6192; Walsh et al., The American Journal of Cardiology (2001) 88:825-828; Watson et al., Experimental Physiology (1999) 84:1013-1022; Weigel and Zhang, J. Mol. Med. (1998) 76:469-479; Whelan et al., Nucleic Acids Research (1991) 19:2645-2653; Zang et al., Journal of Neuroimmunology (2002) 124:106-114;

285. Expert Report of Dr. Stephen Prescott, dated October 21, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-96 attached with this Fourth Supplemental Information Disclosure Statement, namely: U.S. Patent No. 6,410,516, issued June 25 , 2002, Baltimore et al.; Physicians' Desk Reference, 24<sup>th</sup> Ed. (1970) various pages of the Generic and Chemical Name Index; Physicians' Desk Reference 39<sup>th</sup> Ed. (1985) pp.1811-1813; Declaration Under 37 C.F.R. §1.132 by David Baltimore singed September 14, 1999; Examiner's Amendment pps. 2-31; Adams and Teegarden, J. Nutr. (2004) 134:2948-2952; Aljada et al., The Journal of Clinical Endocrinology & Metabolism (1996) 84:3386-3389; Alroy et al., Molecular and Cellular Biology (1995) 15:5789-5799; Auphan et al., Science (1995) 270:286-290; Baeuerle and Baichwal, Advances in Immunology (1997) 65:111-137; Baldwin Jr., A.S., Annu. Rev. Immunol. (1996) 14:649-681; Bantel et al., Am. J. Gastroenterol (2000) 95:3452-3457; Bennett Jr. et al., JAMA (1963) 183:166-169; Bergmann et al., Am. J. Respir. Cell Mol. Biol. (2004) 30:555-563; Bergmann et al., Immunology (2004) 111:430-434; Berry et al., Experimental Cell Research (2002) 272:176-184; Björnström and Sjöberg, Molecular Endocrinology (2005) 19:833-842; Blanco-Colio et

Applicants: David Baltimore et al.  
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Page 71 of 103 of September 28, 2006 Amendment

al., Circulation (2000) 102:1020-1026; Blanco Colio et al., Manuscript; Bochkov et al., Blood (2002) 99:199-206; Brini et al., Eur. Cytokine Net. (1990) 1:131-139; Callejas et al., Hepatology (2002) 35:341-348; Chaudhary and Avioli, The Journal of Biological Chemistry (1996) 271:16591-16596; Cid et al., J. Clin. Invest. (1994) 93:17-25; Delhase et al., Science (1999) 284:309-313; Deshpande et al., AJRI (1997) 38:46-54; Dew et al., British Medical Journal (1983) 287:23-24; Din et al., British Journal of Cancer (2004) 91:381-388; Emmel et al., Science (1989) 246:1617-1620; Curriculum Vitae of Stephen Michael Prescott dated 8/12/05; Synthetic Generic Conjugated Estrogens <<http://www.fda.gov/eder/news/cetimeline.htm>>; Forsblad et al., Arthritis Research & Therapy (2003) 5:R202-R209; Fujihara et al., the Journal of Immunology (2000) 165:1004-1012; Giffin et al., Nature Structural Biology (2003) 10:800-806; Gilmore and Morin, Reviews (1993) 9:427-433; Goodman & Gilman's The Pharmacological Basis of Therapeutics, 9<sup>th</sup> Ed. Pp. 625-631 and 1780 & 1712; Griffith et al., Cardiac Transplantation (1982) 196:324-329; Griffith et al., J. Thorac Cardiovasc Surg. (1984) 88:952-957; Hahn et al., Journal of Clinical Investigation (1950) pp. 274-281; Hämäläinen et al., European Journal of Pharmacology (2002) 448:239-244; Han et al., Rheumatology (2001) 40:267-273; Haynes et al., Circ. Res. (2000) 87:677-682; Ho et al., Clinical Immunology and Immunopathology (1996) 80:S40-S45; Hogan et al. Genes & Development (2003) 17:2205-2232; Holmes-McNary and Baldwin Jr., Cancer Research (2000) 60:3477-3483; Hölschermann et al., The Journal of Immunology (2001) 166:7112-7120; Hölschermann et al., Circulation (1997) 96:4232-4238; Ide and Lau, J. Nutr. (2001) 131:1020S-1026S; Kayisli et al. Biology of Reproduction (2004) 71:714-721; Kim and Leonard, The EMBO

Applicants: David Baltimore et al.  
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Filed : January 4, 2002  
Page 72 of 103 of September 28, 2006 Amendment

Journal (2002) 21:3051-3059; Kinoshita et al., Immunity (1997) 6:235-244; Kopp and Ghosh, Science (1994) 265:956-959; Krönke et al., Proc. Natl. Acad. Sci. USA (1984) 81:5214-5218; Lefering and Neugebauer, Critical Care Medicine (1995) 23:1294-1303; Lemire et al., J. Clin. Invest. (1984) 74:657-661; Lemire et al., The Journal of Immunology (1985) 134:3032-3035; Loh et al., The Journal of Biological Chemistry (1996) 271:10884-10891; Liu et al., The Journal of Biological Chemistry (2002) 277:24353-24360; Manna et al., The Journal of Immunology (2000) 164:6509-6519; Manolagas et al., J. Clin. Endocrinol Metab. (1986) 63:394-400; McCaffrey et al., Nucleic Acids Research (1994) 22:2134-2142; Perez-G. et al., The Journal of Immunology (2002) 168:1428-1434; Nagasawa et al., Journal of Cellular Physiology (1981) 109:181-192; Nagpal et al., Current Medicinal Chemistry (2001) 8:1661-1679; Nelson et al., JAMA (2002) 288:872-881; Park et al., Nephrol Dial Transplant (2004) 19:312-319; Pendurthi et al., Arterioscler Thromb Vasc. Biol. (1999) 19:419-426; Reed et al., The Journal of Immunology (1986) 137:150-154; Rigby et al., J. Clin. Invest. (1984) 74:1451-1455; Rigby et al., The Journal of Immunology (1985) 135:2279-2286; Rovera et al., Science (1979) 204:868-870; Ryu et al., Biochemical and Biophysical Research Communications (2000) 272:758-764; Sadikot et al., Am. J. Respir. Crit. Care Med. (2001) 164:873-878; Scheinman et al., Science (1995) 270:283-286; Scheinman et al., Molecular and Cellular Biology (1995) 15:943-953; Schmidt et al., Journal of Virology (1990) 64:4037-4041; American Association for the Advancement of Science (1993); Sica et al., The Journal of Biological Chemistry (1997) 272:30412-30420; Siebenlist et al., Molecular and Cellular Biology (1986) 6:3042-3049; Siebenlist et al., Annu. Rev. Cell Virol. (1994) 10:405-455; Simoncini et al., Cir. Res.

Applicants: David Baltimore et al.  
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(2000) 87:19-25; Simoncini et al., Nature (2000) 407:538-541; Singh and Aggarwal, J. Of Biological Chemistry (1995) 270:24995-25000; Leger et al., The Lancet (1979) 1:1017-1020; Stark et al., The FASEB Journal (2001) 15:1273-1275; Takeuchi et al., The Journal of Immunology (1998) 160:209-218; Tobler et al., Blood (1992) 79:45-51; Tsoukas et al., Science (1984) 224:1438-1440; Wadsworth and Koop, Biochemical Pharmacology (1999) 57:941-949; Weissmann G., Scientific American (1991) pp. 84-90; Weissmann et al., Abstract (2002) 571-577; Yan and Polk, the Journal of Biological Chemistry (1999) 274:36631-36636; Yang et al., J. Nutr. (1998) 128:2334-2340; Yin et al., Nature (1998) 396:77-80; Yu et al., Proc. Natl. Acad. Sci. USA (1995) 92:10990-10994; Yuan et al., Science (2001) 293:1673-1677;

286. Expert Report of Jeffrey V. Ravetch, M.D., Ph.D., dated October 21, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-96 attached with this Fourth Supplemental Information Disclosure Statement, namely: U.S. Patent 6,410,516, issued June 25, 2002, Baltimore et al.; Physicians' Desk Reference, 24<sup>th</sup> Ed. (1970) various pages of the Generic and Chemical Name Index; Physicians' Desk Reference 39<sup>th</sup> Ed. (1985) pp.1811-1813; Declaration Under 37 C.F.R. §1.132 by David Baltimore singed September 14, 1999; Examiner's Amendment pps. 2-31; Adams and Teegarden, J. Nutr. (2004) 134:2948-2952; Aljada et al., The Journal of Clinical Endocrinology & Metabolism (1996) 84:3386-3389; Alroy et al., Molecular and Cellular Biology (1995) 15:5789-5799; Auphan et al., Science (1995) 270:286-290; Baeuerle and Baichwal, Advances in Immunology (1997) 65:111-137; Baldwin Jr., A.S., Annu. Rev. Immunol. (1996) 14:649-681; Bantel et al., Am. J. Gastroenterol (2000) 95:3452-3457; Bennett Jr. et al., JAMA (1963) 183:166-169;

Applicants: David Baltimore et al.  
Serial No.: 10/037,341  
Filed : January 4, 2002  
Page 74 of 103 of September 28, 2006 Amendment

Bergmann et al., Am. J. Respir. Cell Mol. Biol. (2004) 30:555-563; Bergmann et al., Immunology (2004) 111:430-434; Berry et al., Experimental Cell Research (2002) 272:176-184; Björnström and Sjöberg, Molecular Endocrinology (2005) 19:833-842; Blanco-Colio et al., Circulation (2000) 102:1020-1026; Blanco Colio et al., Manuscript; Bochkov et al., Blood (2002) 99:199-206; Brini et al., Eur. Cytokine Net. (1990) 1:131-139; Callejas et al., Hepatology (2002) 35:341-348; Chaudhary and Avioli, The Journal of Biological Chemistry (1996) 271:16591-16596; Cid et al., J. Clin. Invest. (1994) 93:17-25; Delhase et al., Science (1999) 284:309-313; Deshpande et al., AJRI (1997) 38:46-54; Dew et al., British Medical Journal (1983) 287:23-24; Din et al., British Journal of Cancer (2004) 91:381-388; Emmel et al., Science (1989) 246:1617-1620; Curriculum Vitae of Jeffrey V. Ravetch; Synthetic Generic Conjugated Estrogens <<http://www.fda.gov/eder/news/cetimeline.htm>>; Forsblad et al., Arthritis Research & Therapy (2003) 5:R202-R209; Fujihara et al., the Journal of Immunology (2000) 165:1004-1012; Giffin et al., Nature Structural Biology (2003) 10:800-806; Gilmore and Morin, Reviews (1993) 9:427-433; Goodman & Gilman's The Pharmacological Basis of Therapeutics, 9<sup>th</sup> Ed. Pp. 625-631 and 1780 & 1712; Griffith et al., Cardiac Transplantation (1982) 196:324-329; Griffith et al., J. Thorac Cardiovasc Surg. (1984) 88:952-957; Hahn et al., Journal of Clinical Investigation (1950) pp. 274-281; Hämäläinen et al., European Journal of Pharmacology (2002) 448:239-244; Han et al., Rheumatology (2001) 40:267-273; Haynes et al., Circ. Res. (2000) 87:677-682; Ho et al., Clinical Immunology and Immunopathology (1996) 80:S40-S45; Hogan et al. Genes & Development (2003) 17:2205-2232; Holmes-McNary and Baldwin Jr., Cancer Research (2000) 60:3477-3483; Hölschermann et al., The

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Filed : January 4, 2002  
Page 75 of 103 of September 28, 2006 Amendment

Journal of Immunology (2001) 166:7112-7120; Hölschermann et al., Circulation (1997) 96:4232-4238; Ide and Lau, J. Nutr. (2001) 131:1020S-1026S; Kayisli et al. Biology of Reproduction (2004) 71:714-721; Kim and Leonard, The EMBO Journal (2002) 21:3051-3059; Kinoshita et al., Immunity (1997) 6:235-244; Kopp and Ghosh, Science (1994) 265:956-959; Krönke et al., Proc. Natl. Acad. Sci. USA (1984) 81:5214-5218; Lefering and Neugebauer, Critical Care Medicine (1995) 23:1294-1303; Lemire et al., J. Clin. Invest. (1984) 74:657-661; Lemire et al., The Journal of Immunology (1985) 134:3032-3035; Loh et al., The Journal of Biological Chemistry (1996) 271:10884-10891; Liu et al., The Journal of Biological Chemistry (2002) 277:24353-24360; Manna et al., The Journal of Immunology (2000) 164:6509-6519; Manolagas et al., J. Clin. Endocrinol Metab. (1986) 63:394-400; McCaffrey et al., Nucleic Acids Research (1994) 22:2134-2142; Perez-G. et al., The Journal of Immunology (2002) 168:1428-1434; Nagasawa et al., Journal of Cellular Physiology (1981) 109:181-192; Nagpal et al., Current Medicinal Chemistry (2001) 8:1661-1679; Nelson et al., JAMA (2002) 288:872-881; Park et al., Nephrol Dial Transplant (2004) 19:312-319; Pendurthi et al., Arterioscler Thromb Vasc. Biol. (1999) 19:419-426; Reed et al., The Journal of Immunology (1986) 137:150-154; Rigby et al., J. Clin. Invest. (1984) 74:1451-1455; Rigby et al., The Journal of Immunology (1985) 135:2279-2286; Rovera et al., Science (1979) 204:868-870; Ryu et al., Biochemical and Biophysical Research Communications (2000) 272:758-764; Sadikot et al., Am. J. Respir. Crit. Care Med. (2001) 164:873-878; Scheinman et al., Science (1995) 270:283-286; Scheinman et al., Molecular and Cellular Biology (1995) 15:943-953; Schmidt et al., Journal of Virology (1990) 64:4037-4041; American Association for the Advancement of Science (1993);

Applicants: David Baltimore et al.  
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Page 76 of 103 of September 28, 2006 Amendment

Sica et al., The Journal of Biological Chemistry (1997) 272:30412-30420; Siebenlist et al., Molecular and Cellular Biology (1986) 6:3042-3049; Siebenlist et al., Annu. Rev. Cell Viol. (1994) 10:405-455; Simoncini et al., Cir. Res. (2000) 87:19-25; Simoncini et al., Nature (2000) 407:538-541; Singh and Aggarwal, J. Of Biological Chemistry (1995) 270:24995-25000; Leger et al., The Lancet (1979) 1:1017-1020; Stark et al., The FASEB Journal (2001) 15:1273-1275; Takeuchi et al., The Journal of Immunology (1998) 160:209-218; Tobler et al., Blood (1992) 79:45-51; Tsoukas et al., Science (1984) 224:1438-1440; Wadsworth and Koop, Biochemical Pharmacology (1999) 57:941-949; Weissmann G., Scientific American (1991) pp. 84-90; Weissmann et al., Abstract (2002) 571-577; Yan and Polk, the Journal of Biological Chemistry (1999) 274:36631-36636; Yang et al., J. Nutr. (1998) 128:2334-2340; Yin et al., Nature (1998) 396:77-80; Yu et al., Proc. Natl. Acad. Sci. USA (1995) 92:10990-10994; Yuan et al., Science (2001) 293:1673-1677;

287. Rule 26(A)(2) Report of Bert Spilker, Ph.D., M.D. dated October 21, 2005 in Civil Case 02 CV 11280 RWZ including Exhibit 1 attached with this Fourth Supplemental Information Disclosure Statement, namely: Biography of Dr. Bert Spilker;
288. Rule 26(A)(2) Rebuttal Report of George R. Stark, Ph.D., dated October 21, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-45 attached with this Fourth Supplemental Information Disclosure Statement, namely: U.S. Patent No. 6,060,310, issued May 9, 2000, Cho-Chung; File History of U.S. Serial No. 08/464,364, filed June 5, 1995; U.S. Patent No. 6,410,516, issued June 25, 2002, Baltimore et al.; File History of U.S. Serial No. 07/162,680, March

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1, 1988; File History of U.S. Serial No. 07/280,173, filed December 5, 1988; File History of U.S. Serial No. 07/318,901, filed March 3, 1989; File History of U.S. Serial No. 07/341,436, filed April 21, 1989; Baeuerle and Baltimore, *Cell* (1988) 53:211-217; Baeuerle and Baltimore, *Science* (1988) 242:540-546; Bass et al., *Proteins: Structure, Function & Genetics* (1990) 8:309-314; Berns et al., *Breast Cancer Research & Treatment* (1984) 4:195-204; Boda et al., *Folia Biologica (Praha)* (1987), 33:93-97; Bressler et al., *Journal of Virology* (1993) 67:288-293; Brown et al., *Science* (1995) 267:1485-1488; Cunningham and Wells, *Science* (1989) 244:1081-1085; Davis et al., *Science* (1991) 253:1268-1271; Du et al., *Molecular Brain Research* (2005) 136:177-188; *Curriculum Vitae of George R. Stark*, Ph.D. updated 9/12/05; *Rebuttal Report of George R. Stark*; Fried and Crothers, *Nucleic Acids Research* (1981) 9:6505-6525; Friedman et al., *Nature* (1988) 335:452-454; Gallop et al., *Journal of Medicinal chemistry* (1994) 37:1233-1251; Gesner et al., *Journal of Cellular Physiology* (1988) 136:493-499; Ghosh and Baltimore, *Nature* (1990) 344:678-682; Haskill et al., *Cell* (1991) 65:1281-1289; Horuk R., *Journal of Immunological Methods* (1989) 119:255-258; Hoyos et al., *Science* (1989) 244:457-460; Kawamurn et al., *Gene Therapy* (2001) 8:906-912; Khaled et al., *Clinical Immunology* (1998) 86:170-179; *Methods in Molecular and Cellular Biology* (1989) 1:249; Logeat et al., *The EMBO Journal* (1991) 10:1827-1832; McKinsey et al., *The Journal of Biological Chemistry* (1997) 272:22377-22380; McKnight and Kingsbury, *Science* (1982) 217:316-324; Morishta et al., *Nature Medicine* (1997) 1:894-899; Myers et al., *Research Articles* (1986) 232:613-618; Nabel et al., *Proc. Natl. Acad. Sci. USA* (1996) 93:15388-15393; Nicolau et al., *Cell Cell Fusion* (1984) pp. 254-267; Reisine et al., *Proc. Natl.*

Applicants: David Baltimore et al.  
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Acad. Sci. USA, (1985) 82:8261-8265; Rozemond et al., Immunobiol. (1987) 176:35-46; Sawa et al., Circulation (1997) 96[suppl]:II-280-II-285; Scott and Smith, Science (1990) 249:386-390; Siebenlist et al., Annu. Rev. Cell Biol. (1994) 10:405-455; Tanaka et al., Nucleic Acids Research (1994) 22:3069-3074; Tomita et al., Journal of Hypertension (1996) 16:993-1000; Trepicchio and Krontiris, Nucleic Acids Research (1993) 21:977-985;

289. October 28, 2005 Rule 26(A)(2) Rebuttal Report of Michael Sofocleous, pgs. Cover, 22 and 33, in Civil Case 02 CV 11280 RWZ;
290. November 10, 2005 Eli Lilly and Company's Sixth Supplemental Responses To Plaintiffs' First Set of Interrogatories (Nos. 1-5), pgs. 1-6, in Civil Case 02 CV 11280 RWZ;
291. Reply Expert Report of Peter Barnes, D.M. D.Sc. dated November 11, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-4 attached with this Fourth Supplemental Information Disclosure Statement, namely: Adams et al., Cancer Research (1999) 59:2615-2622; Davis et al., Science (1991) 253:1268-1271; Current Opinion in Cell Biology (1993) 5:477-487; Schmitz et al. Trends in cell Biology (1991) 5:130-137;
292. Rule 26(A)(2) Reply Report of Brendan F. Boyce, M.D. not dated (November 11, 2005) in Civil Case 02 CV 11280 RWZ including Exhibits 1-23 attached with this Fourth Supplemental Information Disclosure Statement, namely: Berkowitz et al., the Journal of Biological Chemistry (2002) 277:24694-24700; Blum et al., the American Journal

Applicants: David Baltimore et al.  
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Filed : January 4, 2002  
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of Cardiology (2000) 86:892-895; Cappellen et al., The Journal of Biological Chemistry (2002) 277:21971-21982; Chadwick et al., PNAS (2005) 102:2543-2548; Chen et al., Nature (1998) 391:410-413; Elices et al., Cell (1990) 60:577-584; Ghisletti et al., Molecular and Cellular Biology (2005) 25:2957-2968; Gianni et al., J. Clin. Endocrinol. Metab. (2004) 89:6097-6099; Harnish et al., Endocrinology (2000) 141:3403-3411; JBMR ASBMR 27<sup>th</sup> Annual Meeting SU103-SU106; Liu et al., J. Natl. Cancer Inst. (2003) 95:1586-1597; Macy et al., Clinical Chemistry (1997) 43:52-58; Marino et al., Molecular and Cellular Endocrinology (2001) 182:19-26; Miller and Harrison, FEBS Letters (1995) 369:113-117; O'Brien et al., Am. J. Physiol. Endocrinol. Metab. (2005) 289:E784-E793; O'Keefe et al., Lab. Invest. (1997) 76:457-465; Reifel-Miller et al., The Journal of Biological Chemistry (1994) 269:23861-23864; Sims et al., J. Clin. Invest. (2004) 113:379-389; Sims et al., J. Bone Miner Res. (2005) 20:1093-1102; Control No. 05-A-1610-ASBMR 1PG.; U.S. Patent No. 6,545,027, issued April 8, 2003, Berg et al.; Walsh et al., The American Journal of Cardiology (2001) 88:825-828; Walsh et al., JAMA (1998) 279:1445-1451;

293. Reply Expert Report of Dr. Jesus Egido dated November 11, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-7 attached with this Fourth Supplemental Information Disclosure Statement, namely: Bertelli et al., Drugs Exptl. Clin. Res. (1998) XXIV:133-138; Buffoli et al., JHC exPress (2005) pp. 2-33; Hai-Hong et al., Journal of the Fourth Military Medical University (2003) 24:923-925; Lee et al., J. Of Clinical Pharmacology (1998) 38:981-993; Kundu and Surh, Mutation Research (2004) 555:65-80; Leiro et al., International Immunopharmacology (2005) 5:393-406; Tsai et

Applicants: David Baltimore et al.  
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al., British Journal of Pharmacology (1999) 126:673-680;

294. Reply Expert Report of Dr. Laurie H. Glimcher dated November 11, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-18 attached with this Fourth Supplemental Information Disclosure Statement, namely: Reply Report of Laurie Glimcher; Brueckmann et al., Thromb. Haemost. (2003) 89:149-160; Brueckmann et al., Inflamm. Res. (2004) 53:528-533; Brun-Buisson et al., JAMA (1995) 274:968-974; Derhaschnig et al., Blood (2003) 102:2093-2098; Dhainaut et al., Thromb. Haemost (2003) 90:642-653; Bernard et al., Intensive Care Med. (2003) 29:894-903; Dhainaut et al., Crit. Care Med. (2004) 32[Suppl]:S194-S201; Joyce et al., The Journal of Biological Chemistry (2001) 276:11199-11203; Joyce et al., Crit. Care Med. (2002) 30[Suppl]:S288-S293; Kalil et al., Shock (2004) 21:222-229; Kinasewitz et al., Critical Care (2004) 8:R82-R90; Martin et al., N. Engl. J. Med. (2003) 348:1546-1554; Nick et al., blood (2004) 104:3878-3885; Opal et al., The Journal of Infectious Diseases (1999) 180:1584-1589; U.S. Patent Application No. US2003/0073632, Published April 17, 2003, Ciaccia et al.; XIGRIS drotrecogin alfa (activated) Drug Action 2pg.; XIGRIS drotrecogin alfa (activated) 1p.;

295. Reply Expert Report of David Latchman, DSc., Ph.D. dated November 11, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-18 attached with this Fourth Supplemental Information Disclosure Statement, namely: Adams et al., Cancer Research (1999) 59:2615-2622; Davis et al., Science (1991) 253:1268-1271; Liou and Baltimore, Current Opinion in Cell Biology (1993) 5:477-487; Schmitz et al. Trends in Cell Biology (1991) 1:130-137;

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296. Rule 26(B)(2) Reply Report of David M. Livingston, M.D. not dated (November 11, 2005) in Civil Case 02 CV 11280 RWZ including Exhibits 1-23 attached with this Fourth Supplemental Information Disclosure Statement, namely: Brueckmann et al., Inflamm. Res. (2004) 53:528-533; Brun-Buisson et al., JAMA (1995) 274:968-974; Chen et al. Nature (1998) 391:410-413; Deraschnig et al., Blood (2003) 102:2093-2098; Dhainaut et al., thromb. Haemost (2003) 90:642-653; Bernard et al., Intensive Care Med. (2003) 29:894-903; Dhainaut et al., Crit. Care Med. (2004) 32[Suppl]:S194-S201; Joyce et al., The Journal of Biological Chemistry (2001) 276:11199-11203; Joyce and Grinnell, Crit. Care Med. (2002) 30[Suppl]:S288-S293; Kalil et al. Shock (2004) 21:222-229; Kinasewitz et al., Critical Care (2004) 8:R82-R90; Marino et al., Molecular and Cellular Endocrinology (2001) 182:19-26; Martin et al., N. Engl. J. Med. (2003) 348:1546-1554; Müller and Harrison, FEBS Letters (1995) 369:113-117; Nick et al., Blood (2004) 104:3878-3885; Opal et al., The Journal of Infectious Diseases (1999) 180:1584-1589; Reifel-Miller et al., The Journal of Biological Chemistry (1994) 269:23861-23864; Control No. 05-A-1610-ASBMR; U.S. Patent Application No. US2003/0073632, Published April 17, 2003, Ciaccia et al.; U.S. Patent No. 5,393,763, issued February 28, 1995, Black et al.; U.S. Patent No. 6,545,027, issued April 8, 2003, Berg et al.; XIGRIS drotrecogin alfa (activated) Drug Action 2pg.; XIGRIS drotrecogin alfa (activated) Emerging Understanding 1pg.;

297. Reply Expert Report of Stavros C. Manolagas, M.D., Ph.D. Regarding Invalidity of the Asserted Claims dated November 11, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-11 attached with this Fourth Supplemental Information

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Disclosure Statement, namely: Declaration of David Baltimore under Rule 1.132 and In re Brana dated February 2001, Castrillo et al., Molecular and Cellular Biology (2000) 20:1692-1698; Gilston et al., Ann. Rheum. Dis. (2000) 59:303-307; Kaltschmidt et al., Biol. Chem. Hoppe-Syler (1995) 376:9-16; Kaltschmidt et al., Proc. Natl. Acad. Sci. USA, (1995) 92:9618-9622; Kumar et al., Oncogene (1998) 17:913-918; LyB et al., the Journal of Biological Chemistry (1998) 273:33508-33516; U.S. Patent No. 5,939,421. Issued August 17, 1999, Palanki et al.; Palombella et al., Proc. Natl. Acad. Sci. USA, (1998) 95:15671-15676; Yan and Polk, the Journal of Biological Chemistry (1999) 274:36631-36636; Zabel et al., The EMBO Journal (1993) 12:201-211;

298. Reply Expert Report of Dr. Stephen Prescott dated November 11, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-25 attached with this Fourth Supplemental Information Disclosure Statement, namely: Reply Report of Stephen Prescott; Blum et al., The American Journal of Cardiology (2000) 86:892-895; Compston, J.E., Physiological Reviews (2001) 81:419-447; Emerick et al., The Pharmacology and Toxicology of Proteins (1987) pgs. 351-367; Further Expert Report of Dr. Dina Stolman dated October 11, 2002; Declaration of Dina Stolman, M.D., M.S.P.H., dated December 18, 2002; Declaration of O. Todd Dickinson dated December 19, 2002; Declaration of Sau-Chi Betty Yan dated December 19, 2002, Declaration of William Macias, M.D., Ph.D., December 19, 2002; Gianni et al., J. Clin. Endocrinol. Metab. (2004) 89:6097-6099; Helvering et al., Molecular Pharmacology (2005) 68:1225-1238; Stein and Yang, Molecular and Cellular Biology (1995) 15:4971-4979; Taranta et al., Bone (2002) 30:368-376; Taylor et al., J. Clin. Invest.

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(1987) 79:918-925; U.S. Patent No. 4,418,068, issued November 29, 1983, Jones; U.S. Patent No. 5,009,889, issued April 23, 1991, Taylor, Jr. et al.; U.S. Patent No. 5,393,763, issued February 28, 1995, Black et al.; U.S. Patent No. 5,457,117, issued October 10, 1995, Black et al.; U.S. File History of Serial No. 08/824,590, filed March 26, 1997; U.S. Patent No. 5,811,120, issued September 22, 1998, Gibson et al., U.S. File History of Serial No. 09/088,695, filed June 1, 1998; U.S. Patent No. 5,972,383, issued October 26, 1999, Gibson et al.; U.S. File History of Serial No. 09/568,146, filed May 10, 2000; U.S. Patent No. 6,489,296, issued December 3, 2002, Grinnell et al.; Walsh et al., The American Journal of Cardiology (2001) 88:825-828;

299. Reply Expert Report of Dr. Jeffrey Ravetch dated November 11, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-21 attached with this Fourth Supplemental Information Disclosure Statement, namely: Reply Report of Jeffrey Ravetch; Blum et al., The American Journal of Cardiology (2000) 86:892-895; Compston, J.E., Physiological Reviews (2001) 81:419-447; Further Expert Report of Dr. Dina Stolman dated October 11, 2002; Declaration of Dina Stolman, M.D., M.S.P.H., dated December 18, 2002; Declaration of O. Todd Dickinson, dated December 19, 2002; Declaration of Sau-Chi Betty Yan, dated December 19, 2002; Declaration of William Macias, M.D., Ph.D., dated December 19, 2002; Gianni et al., J. Clin. Endocrinol. Metab. (2004) 89:6097-6099; Helvering et al., Molecular Pharmacology (2005) 68:1225-1238; Taranta et al., Bone (2002) 30:368-376; Taylor et al., J. Clin. Invest. (1987) 79:918-925; U.S. Patent No. 5,009,889, issued April 23, 1991, Taylor, Jr. et al.; U.S. Patent No. 5,393,763, issued February 28,

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1995, Black et al.; U.S. Patent No. 5,457,117, issued October 10, 1995, Black et al.; File History of U.S. Serial No. 08/824,590, filed March 26, 1997; U.S. Patent No. 5,811,120, issued September 22, 1998, Gibson et al.; File History of U.S. Serial No. 09/088,695, filed June 1, 1998; U.S. Patent No. 5,972,383, issued October 26, 1999, Gibson et al.; U.S. Patent No. 6,489,296, issued December 3, 2002, Grinnell et al.; Walsh et al., The American Journal of Cardiology (2001) 88:825-828;

300. November 11, 2005 Reply Expert Report of Dr. Jeffrey Ravetch, pgs. 1-11, in Civil Case 02 CV 11280 RWZ;
301. November 11, 2005 Reply Expert Report of Dr. Laurie H. Glimcher, pgs. 1-13, in Civil Case 02 CV 11280 RWZ;
302. November 11, 2005 Reply Expert Report of David Latchman, DSc., Ph.D., Document 198, filed 02/03/2006, pgs. 1-58, in Civil Case 02 CV 11280 RWZ;
303. November 18, 2005 Condensed Deposition of Carolyn Smith in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-11 attached with this Third Supplemental Information Disclosure Statement, namely: Cirriculum Vitae of Carolyn Louise Smith, Ph.D., ADL Bates Nos. 0037187-0037205 [DDX 300 11/18/05]; September 8, 2005 Expert Report of Dr. Carolyn L. Smith Restricted Confidential [DDX 301 11/18/05]; November 11, 2005 Declaration of Carolyn Smith [DDX 302 11/18/05]; Laboratory notebook of Dr. Carolyn Smith, Bates Nos. CLS 00001-00295 Confidential Information Under Protective Order [DDX 303 11/118/05]; Cavarretta, et al., Molecular Endocrinology (2002), 16(2):253-270 [DDX 304 11/18/05]; Coleman, et al., The Journal of Biological

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Chemistry, (2003), 278(15):12834-12845 [DDX 305 11/18/05]; Dutertre and Smith, The Journal of Pharmacology and Experimental Therapeutics, (2000), 295(2):431-437 [DDX 307 11/18/05]; Marino et al., Molecular and Cellular Endocrinology, (2001), 182:19-26 [DDX 308 11/18/05]; Smith and Cummings, Supplement to Menopause Management, (March/April 2005), pp. 40-43 [DDX 309 11/18/05]; Abstract SA485-SA488 from Journal of Bone and Mineral Research, (2000), p. S325 [DDX 310 11/18/05]; and Abstract SA473-SA476 from Journal of Bone and Mineral Research (2003), [DDX 311 11/18/05];

304. November 21, 2005 Plaintiffs' Supplemental Responses To Eli Lilly & Co.'s First, Second, Third, and Fourth Sets of Interrogatories (Nos. 2, 3, 6-8), in Civil Case 02 CV 11280 RWZ;
305. November 22, 2005 Condensed Deposition of Stephen Prescott in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-29 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum vitae of Stephen Michael Prescott [DDX 312]; October 21, 2005 Expert Report of Dr. Stephen Prescott [DDX 313]; (the Reply Expert Report of Dr. Stephen Prescott [DDX314] is being submitted under separate cover); November 11, 2005 Reply Expert Report of Stavros C. Manolagas, M.D., Ph.D. Regarding Invalidity of the Asserted Claims [DDX 315]; U.S. Patent No. 6,410,516 B1, issued June 25, 2002, Baltimore et al. [DDX 316]; Tsoukas, Science, (2004), 224:1438-1440 [DDX 317]; Manolagas, et al., Journal of Clinical Endocrinology and Metabolism, (1986), 63(2):394-400 [DX318]; Lemire et al., The Journal of Immunology, (1985), 134(5):3032-3035 [DX319]; Lemire et al., Rapid Publication, (1984), 74:657-

Applicants: David Baltimore et al.  
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661 [DDX320]; Rigby et al., J. Clin. Invest., (1984), 74:1451-1455 [DX321]; Rigby et al., The Journal of Immunology, (1985), 135:2279-2286 [DDX322]; Yu et al., Proc. Natl. Acad. Sci. USA, (1995), 92:10990-10994 [DDX323]; September 9, 2005 Expert Report of Stavros C. Manolagas, M.D., Ph.D. [DDX324]; Declaration of Stavros Manolagas, M.D. Ph.D. [DDX325]; Adams and Teegarden, J. Nutr., (2004), 134:2948-2952 [DDX326]; Berry, et al., Experimental Cell Research (2002), 272:176-184 [DDX327]; Alroy, et al., Molecular and Cellular Biology, (1995), 15:5789-5799 [DDX328]; Nagpal et al., Currnet Medicinal Chemistry (2001), 8:1661-1679 [DDX329]; Takeuchi et al., The Journal of Immunology, (1998), 160:209-218 [DDX330]; Blanco-Colio et al., Circulation, (2000), 102:1020-1026 [DDX331]; Blanco-Colio et al., Manuscript [DDX332]; September 9, 2005 Expert Report of Dr. Jesus Egido [DDX333]; November 11, 2005 Reply Expert Report-Dr. Jesus Egido [DDX334]; Schmidt et al., Journal of Virology, (1990), 64:4037-40441 [DDX335]; Brini et al., Eur. Cytokine Net., (1990), 1:131-139 [DDX336]; Emmel et al., Science (1989), 246:1617-1620 [DDX337]; Yin et al., Nature, (1998), 396:77-80 [DDX338]; Baeuerle and Baichwal, Advances in Immunology, (1997), 65:111-137 [DDX339]; September 7, 2005 Expert Report of Peter Barnes, Ph.D. [DDX340]; and June 8, 2005 Order Granting/Denying Request for Ex Parte Reexamination [DDX341];

306. November 30, 2005 Condensed Deposition of Jeffrey V. Ravetch in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-11 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum vitae of Jeffrey V. Ravetch [342 11/30/05]; October 21, 2005 Expert Report of Jeffrey V. Ravetch, M.D., Ph.D. [343

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11/30/05]; March 3, 2004 Memorandum of Decision And Order [345 11/30/05]; Kopp and Gosh, Science, (1994), 265:956-959 [347 11/30/05]; Kinoshita et al., Immunity, (1997), 6:235-244 [348 11/30/05]; Yan and Polk, The Journal of Biological Chemistry, (1999), 274:36631-36636 [349 11/30/05]; Bantel et al., The American Journal of Gastroenterology, (2000), 95:3452-3457 [350 11/30/05]; Kaltschmidt et al., Biol. Chem. (1995), 376:9-16 [351 11/30/05]; Hölschermann, et al., Circulation, (1997), 96:4232-4238 [352 11/30/05]; Palombella et al., Proc. Natl. Acad. Sci. USA (1998), 95:15671-15676 [353 11/30/05]; and U.S. Patent No. 5,939,421, issued August 17, 1999, Palanki et al. [354 11/30/05];

307. December 9, 2005 Condensed Deposition of George Stark in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-20 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum vitae of George R. Stark, Ph.D. [DDX 356 12/9/05]; October 21, 2005 Rule 26(A)(2) Rebuttal Report Of George R. Stark, Ph.D. [DDX357 12/9/05]; September 9, 2005 Expert Report of David Latchman, DSc., Ph.D. [DDX358 12/9/05]; November 11, 2005 Reply Expert Report Of David Latchman, DSc., Ph.D. [DDX359 12/9/05]; September 9, 2005 Expert Report of Peter Barnes, Ph.D. [DDX360 12/9/05]; File History of U.S. Serial No. 07/341,436, filed April 21, 1989 [DDX370 12/9/05]; Horuk, R., Journal of Immunological Methods, (1989), 119:255-258 [DDX371 12/9/05]; Scott and Smith, Science, (1990), 249:386-390 [DDX372 12/9/05]; File History of U.S. Serial No. 07/280,173. Filed 12/05/88 [DDX373 12/9/05]; Khaled et al., Clinical Immunology and Immunopathology, (1998), 56:170-179 [DDX374 12/9/05]; Tomita et al., J. Hypertens, (1998), 16:993-1000 [DDX375 12/9/05]; Du et al., Molecular

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Brain Research (2005), 136:177-188 [DDX376 12/9/05]; Davis, et al., Science, (1991), 253:1268-1271 [DDX377 12/9/05]; Liou and Baltimore, Current Opinion in Cell Biology, (1993), 5:477-487 [DDX378 12/9/05]; Siebenlist et al., Annul. Rev. Cell Biol. (1994), 10:405-455 [DDX379 12/9/05]; Castrillo et al., Molecular and Cellular Biology, (2000), 20:1692-1698 [DDX380 12/9/05]; Yan and Polk, The Journal of Biological Chemistry, (1999), 274:36631-3636 [DDX381]; Declaration of David Baltimore under Rule 1.132 and In re Brana [DDX382 12/9/05]; March 3, 2004 Memorandum of Decision And Order [DDX383 12/9/05]; and U.S. Patent No. 5,939,421, issued August 17, 1999 Palanki et al., [DDX384 12/9/05];

308. December 9, 2005 Deposition of Dr. George Stark, Document 198, filed 02/03/2006, pgs. 1-5, 128-129, 134-135, 147-148 and 277, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

309. December 12, 2005 Condensed Deposition of Jesus Egido in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-8 attached with this Third Supplemental Information Disclosure Statement, namely: Pasaje de los Aucianos, 24, 28034 Madrid [Egido 1 12/12/05]; Abbreviated Curriculum Vitae of Jesus Egido MD [Egido 2 12/12/05]; September 9, 2005 Expert Report-Dr. Jesus Egido [Egido 3 12/12/05]; Binder of references for J. Edigo which includes: St. Leger et al., The Lancet, (1979), 1017-1020; Manna et al., The Journal of Immunology (2000), 164:6509-6519; Holmes-McNary and Baldwin Jr., Cancer Research (2000), 60:3477-3483; Blanco-Colio, Circulation., (2000), 102:1020-1026; Department of Health & Human Services Public Health

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Applicants: David Baltimore et al.  
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<http://www.nal.usda.gov/fnic/Dietary/dietdor.htm>; Gaziano et al., The New England Journal of Medicine, (1993), 329:1829-1834; Dell'Agli, Cardiovascular Research, (2004), 63:593-602; Bellido et al., Am. J. Clin. Nutr. (2004), 80:1487-1491; Ritchie, M.E., Circulation. (1998), 98:1707-1713; Ghanim et al., Circulation, (2004) 110:1564-1571; Hofman et al., Diabetologia (1999), 42:222-232; Hofman et al., Diabetes Care, (1998), 21:1310-1316; Martin-Ventura et al., Stroke (2004), 35:458-463; Tsang et al., British Journal of Nutrition, (2005), 94:170-181; Tsang et al., Br. J. Nutr. (2005), 2pgs.; Baldwin Jr., A. S., The Journal of Clinical Investigation, (2001), 107:3-6; Deo et al., Journal of the American College of Cardiology, (2004), 44:1812-1818, see Tab 3; Holmes-McNary, see Tab 2. Manna, Lopez-Velez, Critical Reviews in Food Science and Nutrition, (2003), 43:233-244; Burns et al., J. Agric. Food Chem. (2002), 50:4096-4102; Blanco-Colio, Manuscript [Edigo 4 12/12/05; Giugliano, MD, To the Editor and Blanco-Colio et al., Response. [Edigo 5 12/12/05]; November 11, 2005 Reply Expert Report-Dr. Jesus Egido [Edigo 6 12/12/05]; Leiro et al., International Immunopharmacology (2005), 5:393-406 [Edigo 7 12/12/05; and Tsang et al., British Journal of Nutrition, (2005), 93:233-240 [Edigo 8 12/12/05];

310. December 13, 2005 Confidential Deposition of Peter Barnes pgs. 1, 111-125 and 133-136, in Civil Case 02 CV 11280 RWZ;
311. December 13, 2005 Confidential Deposition of Peter Barnes, pp. 1-2, 48-49, 181-182 in Civil Case 02 CV 11280 RWZ;
312. December 14, 2005 Condensed Deposition of David Latchman in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-

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10 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum Vitae of Professor David S. Latchman [Latchman 1 12/14/05]; September 9, 2005 Expert Report of David Latchman, DSc., Ph.D. [Latchman 2 12/14/05]; November 11, 2005 Reply Expert Report of David Latchman, DSc., Ph.D. [Latchman 3 12/14/05]; Hand written note [Latchman 4 12/14/05]; Hand written notes [Latchman 5 12/14/05]; October 21, 2005 Rule 26(A)(2) Rebuttal Report of Thomas R. Kadesch, Ph.D. [Latchman 6 12/14/05]; Hoyos et al., Science (1989), 244:457-460 [Latchman 7 12/14/05]; Horuk, R., Journal of Immunological Methods, (1989), 119:255-258 [Latchman 8 12/14/05]; Scott and Smith, Science, (1990), 249:386-390 [Latchman 9 12/14/05]; and March 3, 2004 Memorandum Of Decision and Order [Latchman 10 12/14/05];

313. December 14, 2005 Deposition of David Latchman, pp. 1-3, 64-65, 174 & 275, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

314. December 16, 2005 Condensed Deposition of Laurie H. Glimcher in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-13 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum Vitae of Laurie H. Glimcher [DDX 385 12/16/05]; Glick and Opal, Review Article Drugs, (2004), 837-859 [DDX388 12/16/05 & Opal 105]; Opal and Huber, Critical Care, (2002), 6:125-136 [DDX389 12/16/05]; Joyce et al., The Journal of Biological Chemistry, (2001), 276:11199-11203 [DDX390 12/16/05]; Joyce and Grinnell, Crit. Care Med, (2002), 30:S288-S293 [DDX391 12/16/05]; Brun-Buisson et al., JAMA, (1995), 274:968-974 [DDX392 12/16/05]; Joyce et al., The Journal of Biological Chemistry, (2001), 276:11199-11203 [DDX393 12/16/05];

Applicants: David Baltimore et al.  
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Brueckmann et al., Inflamm. Res. (2004), 528-533 [DDX394 12/16/05]; Leeuwen et al., Crit Care Med (2001), 29:1074-1077 [DDX395 12/16/05]; Derhaschnig et al., Blood. (2003), 102:2093-2098 [DDX396 12/16/05]; Kalil et al., Chock, (2004), 21:222-229 [DDX397 12/16/05]; Nick et al., Blood, (2004), 104:3878-3885 [DDX398 12/16/05]; Dhainaut, Crit Care Med. (2004) 32Supp:S194-S201 [DDX399 12/16/05];

315. December 17, 2005 Condensed Deposition of Brendan F. Boyce Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-12 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum Vitae of Brendan Franceis Boyce [DDX 400 12/17/05]; Gianni et al., J. Clin. Endocrinol Metab., (2004), 89:6097-6099 [DDX403 12/17/05]; Blum, et al., The American Journal of Cardiology Brief Reports, (2000), 86:892-895 [DDX404 12/17/05]; Walsh et al., The American Journal of Cardiology, (2001), 88:825-828 [DDX405 12/17/05]; Jimi et al., Nature Medicine (2004), 10:617-624 [DDX406 12/17/05]; Compston, J.E., Physiological Reviews, (2001), 31:419-447 [DDX407 12/17/05]; Chadwick et al., PNAS, (2005), 102:2543-2548 [DDX408 12/17/05]; Harnish, et al., Endocrinology, (2000), 141:3403-3411 [DDX409 12/17/05]; U.S Patent No. 6,545,027 B1, issued April 8, 2003, Berg et al. [DDX410 12/17/05]; Reifel-Miller et al., The Journal of Biological Chemistry, (1994), 269:23861-23864 [DDX411 12/17/05]; Chen et al., Nature, (1998), 391:410-413 [DDX415 12/17/05]; Olivier, et al., Presentation Number: SU104 [DDX414 12/17/05];

316. December 20, 2005 Condensed Deposition of Thomas R. Kadesch Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-12 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum Vitae of Thomas

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Robert Kadesch [DDX 414 12/20/05]; October 21, 2005 Rule 26(A) (2) Rebuttal Report of Thomas R. Kadesch, Ph.D. [DDX 415 12/20/05]; September 9, 2005 Expert Report of David Latchman, DSc., Ph.D. [DDX416 12/20/05]; November 11, 2005 Reply Expert Report of David Latchman, DSc., Ph.D. [DDX417 12/20/05]; U.S. Patent No. 5,500,365, issued March 19, 1996 Fischhoff et al. [DDX418 12/20/05]; Horuk R., Journal of Immunological Methods, (1989), 119:255-258 [DDX419 12/20/05]; Gehrt, et al., The Journal of Antibiotics, (1998), 51:455-463 [DDX420 12/20/05]; Kumar et al., Oncogene (1998), 17:913-918 [DDX421 12/20/05]; Davis et al., Science, (1991), 253:1268-1271 [DDX422 12/20/05]; Haskill et al., Cell, (1991), 65:1281-1289 [DDX423 12/20/05]; Bielinska et al., Science, (1990), 250:997-1000 [DDX424 12/20/05]; Hoyos et al., Science, (1989), 244:457-460 [DDX425 12/20/05];

317. December 20, 2005 Videotaped Deposition of Thomas R. Kadesch, pgs. 1-4, 138, 196, 269, 297-299, 307-308 and 332, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
318. December 22, 2005 Condensed Transcript of Videotaped Deposition of Stavros C. Manolagas in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1, and 3-19 attached with this Supplemental Information Disclosure Statement, namely: September 9, 2005 Expert Report of Stavros C. Manolagas [Manolagas 12/22/05 Exh 1]; November 11, 2005 Reply Expert Report of Stavros C. Manolagas, M.D. Ph.D. Regarding Invalidity of the Asserted Claims [Manolagas 12/22/05 Exh 3]; Declaration of Stavros Manolagas, M.D. Ph.D. [Manolagas 12/22/05 Exh 4]; Curriculum Vitae of Stavros C. Manolagas, M.D., Ph.D. last

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updated 12/19/05 [Manolagas 12/22/05 Exh 5]; Kousteni et al., The Journal of Clinical Investigation (June 2003) Vol. 111, No. 11, pp. 1651-1664 [Manolagas 12/22/05 Exh 6]; Physicians' Desk Reference, 39 Ed. (1985) p. 1811-1813 [Manolagas 12/22/05 Exh 7]; Emmel et al., Science (1989) 246:1617-1620 [Manolagas 12/22/05 Exh 8]; Brini et al., Eur. Cytokine Net. (Aug.-Sept. 1990) Vol. 1, No. 3, pp. 131-139 [Manolagas 12/22/05 Exh 9]; Schmidt et al., Journal of Virology (Aug. 1990) Vol. 64, No. 8, pp. 4037-4041 [Manolagas 12/22/05 Exh 10]; Krönke et al., Proc. Natl. Acad. Sci. USA (Aug. 1984) 81:5214-5218 [Manolagas 12/22/05 Exh 11]; Adams and Teegarden, J. Nutr. (2004) 134:2948-2952 [Manolagas 12/22/05 Exh 12]; Ho, S. et al., Clinical Immunology and Immunopathology (1996) Vol. 80, No. 3, pp. S40-S45 [Manolagas 12/22/05 Exh 13]; Johansen et al., J. Invest Dermatol (2005) 124:1284-1292 [Manolagas 12/22/05 Exh 14]; File History of U.S. Serial No. 08/474,936, filed June 7, 1995 [Manolagas 12/22/05 Exh 15]; Harnish et al., Endocrinology (2000) Vol. 141, No. 9, pp. 3403-3411 [Manolagas 12/22/05 Exh 16]; Ghisletti et al., Molecular And Cellular Biology (2005) Vol. 25, No. 8, pp. 2957-2968 [Manolagas 12/22/05 Exh 17]; U.S. Patent No. 6,410,516 B1, issued June 25, 2002 Baltimore et al. [Manolagas 12/22/05 Exh 18]; November 11, 2005 Declaration of Carolyn Smith [Manolagas 12/22/05 Exh 19];

319. December 22, 2005 Videotaped and Oral Deposition of Stavros C. Manolagas, pgs. 1-3, and 208-209, Document 198, filed 02/03/2006 in Civil Case 02 CV 11280 RWZ;
320. December 23, 2005 Condensed Deposition of David M. Livingston Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-6 attached with this Third Supplemental

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Information Disclosure Statement, namely: Curriculum Vitae of David Morse Livingston [Livingston 450 12/23/05]; Bernard et al., The New England Journal of Medicine, (2001), 344:699-709 [Livingston 453 12/23/05]; Gianni et al., J. Clin. Endocrinol. Metab., (2004), 89:6097-6099 [Livingston 454 12/23/05]; Taranta, et al., Bone, (2002) 30-368-376 [Livingston 455 12/23/05]; Blum, et al, The American Journal of Cardiology, (2000), 86:892-895 [Livingston 456 12/23/05]; Smith, C.L., Supplement of Menopause Management, (March/April 2005), ppg. 40-43 [Livingston 465 12/23/05];

321. December 23, 2005 Declaration of Lawrence R. Robins In Support Of Defendant Eli Lilly and Company's Motion For Summary Judgment of Invalidity Under 35 U.S.C. §102 including Exhibits 1-13 in Civil Case 02 CV 11280 RWZ;
322. December 23, 2005 Declaration of Lawrence R. Robins in Support of Defendant Eli Lilly and Company's Motion For Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph, including Exhibits A-N in Civil Case 02 CV 11280 RWZ;
323. December 23, 2005 Defendant Eli Lilly and Company's Motion For Summary Judgment of Invalidity Under 35 U.S.C. §§ 101 and 112, First Paragraph in Civil Case 02 CV 11280 RWZ;
324. December 23, 2005 Defendant Eli Lilly and Company's Memorandum In Support of Its Motion For Summary Judgment of Invalidity Under 35 U.S.C. §102 in Civil Case 02 CV 11280 RWZ;
325. December 23, 2005 Defendant Eli Lilly and Company's Motion

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326. December 23, 2005 Defendant Eli Lilly and Company's Rule 56.1 Statement In Support of Its Motion For Summary Judgment of Invalidity Under 35 U.S.C. §102 in Civil Case 02 CV 11280 RWZ;
327. December 23, 2005 Memorandum In Support of Defendant Eli Lilly And Company's Motion For Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph filed under seal pursuant to parties' stipulated protective order in Civil Case 02 CV 11280 RWZ;
328. December 23, 2005 Defendant's Rule 56.1 Statement In Support of Its Motion for Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph in Civil Case 02 CV 11280 RWZ;
329. January 17, 2006 Eli Lilly and Company's Renewed Motion To Stay This Litigation Pending Reexamination of the '516 Patent-In Suit in Civil Case 02 CV 11280 RWZ;
330. January 17, 2006 Memorandum In Support of Eli Lilly and Company's Renewed Motion To Stay This Litigation Pending Reexamination of the '516 Patent-In Suit including Exhibits A-T in Civil Case 02 CV 11280 RWZ;
331. January 25, 2006 Condensed Deposition of Robert Lindsay Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-14 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum Vitae of Robert Lindsay [Lindsay 1 1/25/06]; March 3, 2004 Memorandum of

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Decision And Order [Lindsay 4 1/25/06]; December 21, 2005  
Eli Lilly and Company To Pay U.S. \$36 Million Relating To  
Off-Label Promotion [Lindsay 5 1/25/06]; Cosman and  
Lindsay, Endocrine Reviews, (1999), 20:418-434 [Lindsay 6  
1/25/06]; Kousteni et al., J. Clin. Invest. (2003),  
111:1651-1664 [Lindsay 7 1/25/06]; Helvering et al.,  
Molecular Pharmacology, (2005), 63:1225-1238 [Lindsay 8  
1/25/06]; 71:-77. Of deposition [Lindsay 9 1/25/06]; Walsh  
et al., the American Journal of Cardiology, (2001), 88:825-  
828 [Lindsay 10 1/25/06]; Gianni, et al., J. Clin.  
Endocrinol. Metab., (2004), 89:6097-6099 [Lindsay 11  
1/25/06]; Blum et al., The American Journal of Cardiology,  
(2000), 86:892-895 [Lindsay 12 1/25/06]; U.S. Patent NO.  
4,418,068, issued November 29, 1983, Jones [Lindsay 13  
1/25/06]; Bone and Health and Osteoporosis: A Report of the  
Surgeon General 2004, Executive Summary  
[http://www.surgeongeneral.gov/library/bonehealth/Executive\\_summary.html](http://www.surgeongeneral.gov/library/bonehealth/Executive_summary.html) [Lindsay 14 1/25/06]; Bone Health and  
Osteoporosis Chapter 9 pp219-253 [Lindsay 15 1/25/06]; U.S.  
Patent No. 6,545,027 B1, issued April 8, 2003, Berg et al.  
[Lindsay 16 1/25/06];

332. January 31, 2006 Declaration of Peter Barlett Bressler, M.D., Document 198, filed 02/03/2006 in Civil Case 02 CV 11280 RWZ;
333. January 31, 2006 Plaintiffs' Memorandum In Opposition To Eli Lilly and Company's Renewed Motion To Stay This Litigation Pending Reexamination Of the '516 Patent-In Suit including Exhibits 1-7 and 8A-8I, Document 194, filed 01/31/2006, in Civil Case 02 CV 11280 RWZ;
334. February 1, 2006 First Declaration of Jeffrey V. Ravetch,

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MD, Ph.D., Document 198, filed 02/03/2006, in Civil Case 02  
CV 11280 RWZ;

335. February 1, 2006 Second Declaration of Jeffrey Ravetch  
M.D., Ph.D., Document 201, filed 02/03/2006, in Civil Case  
02 CV 11280 RWZ;
336. February 3, 2006 Concise Statement of Material Facts As to  
Which There Is A Genuine Issue In Support Of Plaintiff's  
Opposition To Lilly's Motion For Summary Judgment of  
Invalidity Under 35 U.S.C. §102, Document 202, filed  
02/03/2006, in Civil Case 02 CV 11280 RWZ;
337. February 3, 2006 Declaration of Vladimir V. Drozdoff In  
Support of Plaintiffs' Opposition to Defendant Eli Lilly &  
Co.'s Motion For Summary Judgment of Invalidity Under 35  
U.S.C. section 102 and Related Documents, Document 203,  
filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
338. February 3, 2006 Declaration of Vladimir V. Drozdoff in  
Support of Plaintiffs' Opposition to Defendant Eli Lilly &  
Co.'s Motion For Summary Judgment of Invalidity Under 35  
U.S.C. Section 101 and 112, First Paragraph, Document 200,  
filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
339. February 3, 2006 Plaintiffs' Opposition to Defendant Eli  
Lilly & Co.'s Motion For Summary Judgment of Invalidity  
Under 35 U.S.C. §§101 and 112, First Paragraph filed under  
seal, Document 198-1, filed 02/03/2006, in Civil Case 02 CV  
11280 RWZ;
340. February 4, 2006 Plaintiffs' Memorandum In Opposition To  
Defendant Eli Lilly & Co.'s Motion For Summary Judgment of

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Invalidity Under 35 U.S.C. Section 102 filed under seal,  
Document 201-1, filed 02/03/2006, in Civil Case 02 CV 11280  
RWZ;

341. February 24, 2006 Declaration of Leslie A. McDonell in Support of Defendant Eli Lilly and Company's Reply Memorandum In Support of Its Motion For Summary Judgment of Invalidity Under 35 U.S.C. §102, Document 214-1, filed 02/24/2006, in Civil Case 02 CV 11280 RWZ;
342. February 24, 2006 Declaration of Leslie A. McDonell in Support of Defendant Eli Lilly and Company's Reply Memorandum In Support of Its Motion For Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph, Document 211, filed 02/24/2006, in Civil Case 02 CV 11280 RWZ;
343. February 24, 2006 Motion For Leave To File Reply Memorandum In Support Of Defendant Eli Lilly and Company's Motion For Summary Judgment Of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph, Document 210-1, filed 02/24/2006, in Civil Case 02 CV 11280 RWZ;
344. February 24, 2006 Reply Memorandum In Support of Defendant's Motion For Summary Judgment Of Invalidity Under 35 U.S.C. §102, Document 213-2, filed 02/24/2006, in Civil Case 02 CV 11280 RWZ;
345. February 24, 2006 Reply Memorandum In Support of Defendant's Motion for Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph, Document 210-2, filed 02/24/2006, in Civil Case 02 CV 11280 RWZ;

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346. March 3, 2006 Plaintiffs' Opposition To Defendant Eli Lilly & Co.'s Motion For Leave To File A Reply Brief In Support of its Summary Judgment of Invalidity Under 35 U.S.C. Section 102 including Exhibit 1, Document 218, filed 03/03/2006, in Civil Case 02 CV 11280 RWZ;

347. March 3, 2006 Concise Statement Of Material Facts As To Which There Is A Genuine Issue In Support of Plaintiffs Opposition to Defendant Eli Lilly & Company's Motion for Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph, Document 199, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

348. March 3, 2006 Plaintiffs Opposition to Defendant Eli Lilly & Company's Motion For Leave To File Reply Memorandum In Support Of Eli Lilly and Company's Motion for Summary judgment of Invalidity under 35 U.S.C. §§101 and 112, First Paragraph, Document 217, filed 03/03/2006, in Civil Case 02 CV 11280 RWZ;

349. March 12, 2006 Condensed Transcript of Videotaped Deposition of Stavros Manolagas, M.D., Ph.D. Vol. II in Civil Case 02 CV 11280 RWZ including deposition Exhibits 22-33 attached with this Supplemental Information Disclosure Statement, namely: Helvering et al., Pharmacol (2005) Vol. 68, No. 5, pp. 1225-1238 [Manolagas 03/12/06 Exh 22]; Taranta et al., Bone (2002) Vol. 30, No. 2, pp. 368-376 [Manolagas 03/12/06 Exh 23]; Expert Report of Jeffrey V. Ravetch, M.D., Ph.D. [Manolagas 03/12/06 Exh 24]; Yu, X-P. et al., Proc. Natl. Acad. Sci, USA (1995) 92:10990-10994 [Manolagas 03/12/06 Exh 25]; Manolagas et al., J. Clin. Endocrinol Metab (1986) Vol. 63, No. 2, pp. 394-400 [Manolagas 03/12/06 Exh 26]; Tsoukas, Science

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(1984) 224:1438-1440 [Manolagas 03/12/06 Exh 27]; Galdiero et al., Microbiology (2001) 147:2697-2704 [Manolagas 03/12/06 Exh 28]; Yang et al., Nature (1998) 395:284-288 [Manolagas 03/12/06 Exh 29]; Prager, Eur. J. Haematology (1997) 59:162-170 [Manolagas 03/12/06 Exh 30]; Lamon-Fava et al., Arterioscler Thromb Vasc Biol. (1999) 19:2960-2965 [Manolagas 03/12/06 Exh 31]; Marino et al., Molecular and Cellular Endocrinology (2001) 182:19-26 [Manolagas 03/12/06 Exh 32]; Reifel-Miller et al., The Journal of Biological Chemistry (1994) 269:23861-23864 [Manolagas 03/12/06 Exh 33];

350. Trial Transcript - April 10, 2006 Jury Trial Day 1, First Session pgs. 1-61, Word Index pgs. 1-10, Second Session pgs. 62-115, Word Index pgs. 1-12, in Civil Case 02 CV 11280 RWZ;
351. Trial Transcript - April 11, 2006 Jury Trial Day 2, First Session pgs. 1-66, Word Index 1-13, Second Session pgs. 66-131, Word Index 1-13, in Civil Case 02 CV 11280 RWZ;
352. Trial Transcript - April 12, 2006 Jury Trial Day 3, First Session pgs. 1-67, Word Index 1-12, Second Session pgs. 68-125, Word Index 1-10, in Civil Case 02 CV 11280 RWZ;
353. Trial Transcript - April 13, 2006 Jury Trial Day 4, First Session pgs. 1-71, Word Index 1-12, Second Session pgs. 72-1128, Word Index 1-10, in Civil Case 02 CV 11280 RWZ;
354. Trial Transcript - April 14, 2006 Jury Trial Day 5, First Session pgs. 1-71, Word Index 1-13, Second Session pgs. 72-122, Word Index 1-10, in Civil Case 02 CV 11280 RWZ;

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355. Trial Transcript - April 18, 2006 Jury Trial Day 6, First Session pgs. 1-91, Word Index 1-16, Second Session pgs. 92-171, Word Index 1-16, in Civil Case 02 CV 11280 RWZ;
356. Trial Transcript - April 19, 2006 Jury Trial Day 7, First Session pgs. 1-106, Word Index 1-18, Second Session pgs. 107-174, Word Index 1-14, in Civil Case 02 CV 11280 RWZ;
357. Trial Transcript - April 20, 2006 Jury Trial Day 8, First Session pgs. 1-89, Word Index 1-14, in Civil Case 02 CV 11280 RWZ;
358. Trial Transcript - April 20, 2006 Jury Trial Day 8, Second Session pgs. 90-157, in Civil Case 02 CV 11280 RWZ;
359. April 20, 2006 Complaint For Declaratory Judgment of Patent Invalidity And Non-Infringement, *Amgen, Inc. et al. v. Ariad Pharmaceuticals, Inc.*, Civil Case 06 CV 00259- KAJ;
360. Trial Transcript - April 21, 2006 Jury Trial Day 9, First and Second Sessions pgs. 1-143, in Civil Case 02 CV 11280 RWZ;
361. Trial Transcript - April 24, 2006 Jury Trial Day 10, First and Second Session pgs. 1-152 and Word Index pgs. 1-22, in Civil Case 02 CV 11280 RWZ;
362. Trial Transcript - April 25, 2006 Jury Trial Day 11, First and Second Session pgs. 1-158 and Word Index pgs. 1-25, in Civil Case 02 CV 11280 RWZ;
363. Trial Transcript - April 26, 2006 Jury Trial Day 12, First and Second Session pgs. 1-156 and Word Index pgs. 1-14,

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Second Session pgs. 88-156 and Word Index pgs. 1-14, in Civil Case 02 CV 11280 RWZ;

364. Trial Transcript - April 27, 2006 Jury Trial Day 13, First Session pgs. 1-86, in Civil Case 02 CV 11280 RWZ;

365. Trial Transcript - April 27, 2006 Jury Trial Day 13, Second Session pgs. 88-141, in Civil Case 02 CV 11280 RWZ;

366. Trial Transcript - April 28, 2006 Jury Trial Day 14, First Session pgs. 1-45, Word Index 1-10, Second Session pgs. 46-130, Word Index 1-17, in Civil Case 02 CV 11280 RWZ;

367. Jury Questions - April 2, 2006 pgs. 1-27, Word Index pgs. 1-5, in Civil Case 02 CV 11280 RWZ;

368. Jury Questions - April 3, 2006 pgs. 1-7, Word Index pgs. 1-2, in Civil Case 02 CV 11280 RWZ;

369. Transcript of Verdict of Jury Trial, Day 18, May 4, 2006 pgs;

370. M. Grieve, Garlic, Botanical.com [online], [retrieved on 2002-08-16], from the Internet <URL:<http://www.botanical.com/botanical/mgmh/g/garlic06.html>>;

371. The Glorious Tea, the origins of tea [online], [retrieved on 2002-08-16], retrieved from Internet: <URL:<http://www.tea.co.uk/tGloriousT/index.htm>>;

372. Curcuma longa Common Name: Tumeric, Nutrisana.com [online], [retreived on 2002-08-16], retrieved from the Internet:

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<URL:<http://www.nutrisana.com/html/Monograph-Curcuma.html>>;

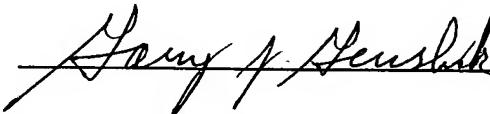
373. Bayer, Questions and Facts, [online], [retrieved on-unknown];

374. Undated Declaration of Stavros Manolagas, M.D. Ph.D. in Reexamination Control No. 90/007,503, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ; and

375. Claims from U.S. Serial No. 07/341,438, filed April 21, 1989, in Civil Case 02 CV 11280 RWZ.

No fee, other than the enclosed \$1,205.00 for a five-month extension of time and excess claim fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

  
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